THE EFFECT OF NEW DRUG EXPOSURE VERSUS A DRUG FREE INTERVAL ON PRIOR DRUG RESISTANCE IN OVARIAN CANCER

by

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Abstract

Continuous exposure of ovarian tumours to a chemotherapy drug can result in the acquisition of drug resistance, which ultimately leads to chemotherapy failure and the death of a great majority of ovarian cancer patients. While previous studies suggest that withdrawal of the chemotherapy drug for a period of time (the drug-free interval) can result in restored clinical sensitivity to the drug, it is unclear whether exposure to a new drug of contrasting mechanism of action may accelerate restored sensitivity to the prior drug. In this study, we exposed a carboplatin-resistant ovarian tumour cell line ($A2780_{CBN}$) to increasing concentrations of docetaxel ($A2780_{CBN \rightarrow DXL}$ cells) or we permitted the cells to grow in the absence of drug for an identical number of drug passages ($A2780_{CBN \rightarrow CC}$ cells). Similarly, we exposed a docetaxel-resistant ovarian tumour cell line ($A2780_{DXL}$) to increasing concentrations of carboplatin ($A2780_{DXL \rightarrow CBN}$ cells) or we permitted the cells to growth in the absence of drug for an identical period ($A2780_{DXL \rightarrow CC}$ cells). By measuring the sensitivity of the above cell lines to either carboplatin or docetaxel, the aim of my thesis studies was to compare the effects of a drug-free interval or the acquisition of new drug resistance on prior drug resistance *in vitro*. The results showed that the prior carboplatin resistance was not significantly altered by the acquisition of docetaxel resistance or by withdrawal of carboplatin. However, prior docetaxel resistance was greatly reduced by selection for carboplatin resistance or by prolonged docetaxel withdrawal. Microarray analysis suggests that the loss of docetaxel resistance may be related to down-regulated expression of the *ABCB1* and *ABCB4* genes, which encode multidrug transporters. It may also relate to up-regulation of *CYP1B1* gene expression, which encodes cytochrome P450, a phase I enzyme involved in taxane metabolism. The microarray analysis data also suggests that the newly established carboplatin

resistance in $A2780_{DXL \rightarrow CBN}$ cells may be related to the expression of genes that promote cell survival by protecting cells from apoptotic death.

Keywords

Docetaxel, Carboplatin, Ovarian Cancer, A2780, Acquired drug resistance, Drug-free interval; Clonogenic Assay, Microarray

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List of Abbreviations

A2780 - parent ovarian carcinoma cell line

$A2780_{CBN}$ - carboplatin resistant ovarian carcinoma cell line

$A2780_{CBN \rightarrow CC}$ - carboplatin resistant ovarian carcinoma cell line cultured in drug free medium

$A2780_{CBN \rightarrow DXL}$ -carboplatin resistant ovarian carcinoma cell line selected for docetaxel resistance

$A2780_{DXL}$ - docetaxel resistant ovarian carcinoma cell line

$A2780_{DXL \rightarrow CBN}$ -docetaxel resistant ovarian carcinoma cell line selected for carboplatin resistance

$A2780_{DXL \rightarrow CC}$ - carboplatin resistant ovarian carcinoma cell line cultured in drug free medium

ABC - ATP binding cassette

Apaf-1 - Apoptotic protease activating factor 1

ATP7A - ATPase, Cu^{2+} transporting, alpha polypeptide

ATP7B - ATPase, Cu^{2+} transporting, beta polypeptide Bcl-2 - B-cell lymphoma 2

ATR - serine/threonine kinase

Bcl-X_L - B-cell lymphoma-extra large

BER - base excision repair

cDNA - complementary DNA

Chk1- Checkpoint kinase 1

cRNA - complementary RNA

CTR1 - copper transporter 1

Cy3 - cyanine 3 dye

Cy5 - cyanine 5 dye

CYP3A - cytochrome P450, family 3, subfamily A

DMSO - dimethyl sulfoxide

DNA - deoxyribonucleic acid

ECM - extracellular matrix

EDTA - ethylenediaminetetraacetic acid

EMT - epithelial mesenchymal transition

EOC - epithelial ovarian cancer

ESCC - esophageal squamous cell carcinoma

FBS - fetal bovine serum

FDR - false detection rate

Glu-Cys-Gly - Glutamine- Cysteine- Glycine

GSH - glutathione

GST - glutathione-*S*-transferase

HIF-1 - hypoxia inducible factor 1

HMG - high mobility group

hUBF - human upstream binding factor

IC50 - inhibitory concentration of drug causing 50% death of a cell population

i.p. - intraperitoneal

i.v. - intravenous

JNK/SAPKs - c-Jun N- terminal kinases/ stress-activated protein kinases

MDR1 - multi-drug resistance gene

mM - milli-molar

mRNA - messenger RNA

MTD - maximally tolerated dose

MTT - 3-(4, 5-dimethylthiazol-2-yl) 2, 5-diphenyl-tetrazolium bromide

NADPH - Nicotinamide adenine dinucleotide phosphate

NER - nuclear excision repair

P-gp - p-glycoprotein

qPCR – quantitative polymerase chain reaction

RIN – RNA integrity number

RNA - ribonucleic acid

ROS - reactive oxygen species

S.E.M - standard error of mean

SRB - sulforhodamine B

TBP - TATA-binding protein

TCF-1a - T cell factor 1

VDAC - voltage-dependent anion channel

Chapter 1

1. Introduction

Ovarian cancer has a high death rate for multiple reasons [1,2]. Firstly, it is often detected and diagnosed at an advanced stage, which is hard to treat. Typically, the disease is treated first by surgery, followed by adjuvant chemotherapy, although neoadjuvant chemotherapy regimens have been employed in some clinical settings [3–5]. The extent of surgery and the choice of chemotherapeutic agents vary depending upon the stage of the tumour. Among the many antitumour agents, extensive studies have been done to elucidate their different mechanisms of action in cancer cells. Secondly, tumour cells can develop resistance to chemotherapeutic drugs, meaning that the tumour is no longer sensitive to the administered drugs [6,7]. Therefore, curability of ovarian cancer is seldom seen. In this chapter, an overview of ovarian cancer, including current treatment regimens and mechanisms of chemotherapy resistance will be discussed.

1.1 Ovarian Cancer

Ovarian cancer has the highest mortality rate among all female gynecological cancers. It is still considered to be the fifth leading cause of death for female cancer patients in North America, and sixth in Europe[1,2]. When ovarian tumours are in an early stage (Stage I), patients present no symptoms, which makes it difficult to discover. At this stage, studies have shown that the 5 year survival rate after treatment can reach as high as 90% [2]. However, most cases of ovarian cancer are usually detected at an advanced stage (Stage III, IV) when the malignancy spreads beyond the ovary and obvious symptoms are exhibited[8,9]. These symptoms, however, are often attributed

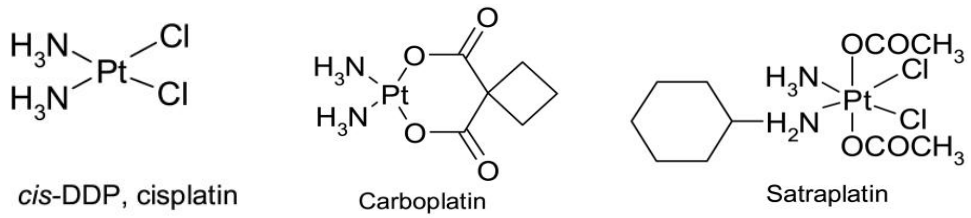
to those preceding or occurring during menstruation or menopause, and are thus overlooked. According to statistics, the 5 year survival rate for stage III or stage IV ovarian cancer drops drastically to around 20% [10–12].

The treatment of ovarian cancer involves both surgery and chemotherapy. At an early stage, after a staging procedure [2], the treatment strategy involves surgery which may be followed by adjuvant chemotherapy [3], depending on the grade of the tumour [13,14]. The agents that are used range from the traditional alkylating agents (cyclophosphamide, thiotepa, melphalan, and bulsulfan)[15,16] to more recently platinating agents (cisplatin, carboplatin, satraplatin) [17]. While platinum-based agents remained first-line chemotherapeutic agents against ovarian cancer in the 1990's, a series of clinical trials in the early 2000's favored the combination of taxanes with platinating agents in the treatment of ovarian cancer [18–21]. In advanced stages of ovarian cancer, the initial responsiveness to combination therapy is as high as 70%. While a combination of taxanes and platinating agents has become a mainstream therapy in ovarian cancer treatment, there is still a high recurrence rate. This is likely due to the acquisition of strong tumour resistance to both drugs, leading to chemotherapy failure. Nowadays, apart from chemotherapeutic agents, a number of biological and targeted therapies have been studied for improving outcomes for ovarian cancer [22], but prognosis remains poor for the disease [23].

1.2 Chemotherapeutic Agents and Their Cytotoxicity

1.2.1 Platinating Agents and Cytotoxicity

Platinating agents are platinum-based drugs including the first generation cisplatin, the less toxic carboplatin, satraplatin, and many other analogues (Figure 1.1).



(A) (B) (C)

Figure 1.1 Chemical structures of platinating agents

Chemical structures of (A) Cisplatin, (B) Carboplatin, and (C) Satraplatin (taken from reference 24).

Platinating agents are commonly used for the treatment of ovarian, lung, testicular, and head and neck cancers [25]. The drug molecules contain leaving groups (e.g. chloride ions in cisplatin, and bidentate dicarboxylate ligands in carboplatin), which are replaced by water molecules in the cytoplasm once the drugs enter the cell. Thus, the hydrolyzed molecules become positively charged and are able to bind to nucleophilic DNA at the N7 atom of purines within the DNA structure [26,27]. The resulting adducts can be grouped into 4 major categories [24]. First, intrastrand adducts form when the platinum-based molecule cross-links with adjacent guanines, both adenine and guanine, or adjacent adenines. Second, this kind of crosslink can also form between two purines from both DNA strands, thus giving rise to interstrand adducts. Other than linkage between nucleobases, protein and DNA adducts can also be facilitated by platinating agents. Last, monoadducts can rarely form when one arm of the molecule forms a linkage to one nucleobase, while the other remains hydrolyzed. The majority of the cross-links are intrastrand adducts, especially ones between adjacent guanines (1, 2-d (GpG)) (Figure 1.2).

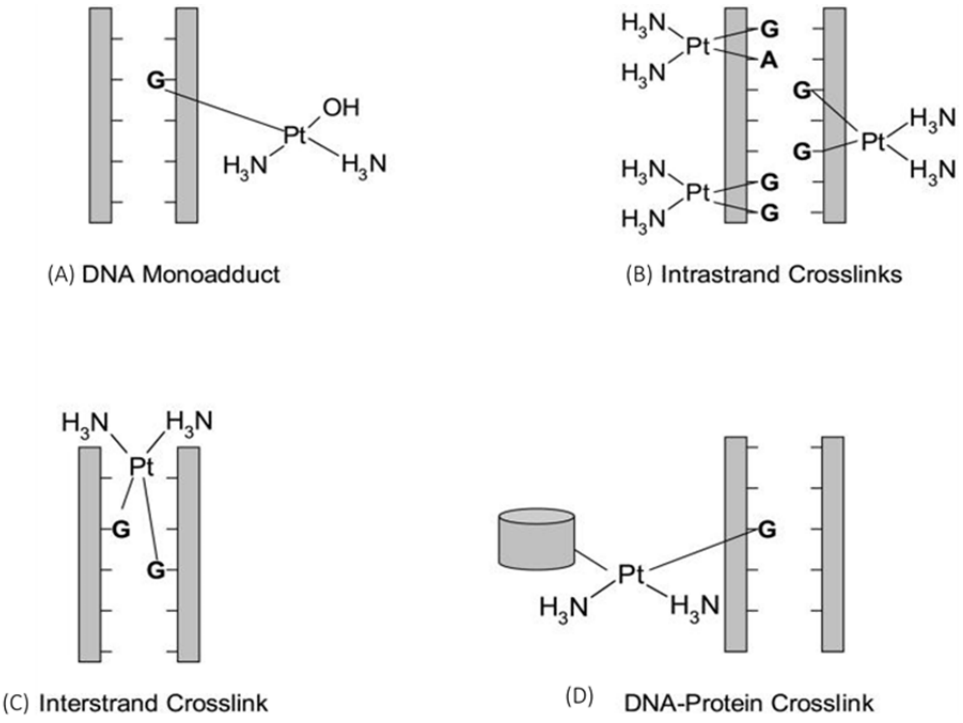


Figure 1.2 Demonstration of platinum-DNA adducts

Demonstration of (A) monoadducts, (B) intrastrand crosslinks, (C) interstrand crosslinks, and (D) DNA-protein crosslinks formed by platinating agents (taken from reference 24).

The strong crosslinks result in the bending and distortion of DNA structure. Hence, disruption of DNA replication, DNA repair and DNA transcription occurs [28,29]. Physically, DNA and RNA polymerases cannot access their normal binding sites to promote DNA replication and transcription, respectively. Moreover, a wide range of proteins has been identified that recognize DNA-cisplatin adducts. One notable category is the HMG (high mobility group) domain proteins[30] (e.g. HMG-1, HMG-2, TCF-1a) that bind DNA-cisplatin adducts. Their binding not only hinders DNA replication but also inhibits the repair of DNA performed by the human excision nuclease and other proteins [31,32]. Other than HMG domain proteins, H1 histones were

also discovered to strongly bind to these DNA adducts, which have been shown to impact on the epigenetic regulation of gene expression [33]. Another mechanism accounting for transcription inhibition is the interference with transcription factor binding to gene promoters [34,35]. The human RNA polymerase I transcription upstream binding factor (hUBF), and TATA binding protein (TBP) are essentially involved in initiation of transcription. DNA adducts formed by cisplatin have been found to sequester these factors at the damaged sites and prevent the transcription process[36,37].

When DNA is damaged by cisplatin, forming bulky crosslinks with DNA, the replication fork is stalled and recruits the damage recognition proteins mentioned above (HMG domain proteins, H1 histone, hUBF, and TBP). Cell cycle progression is then delayed (cell cycle arrest) to repair the damage or to induce a form of programmed cell death termed apoptosis [38]. One typical pathway induced by DNA adduct formation is the ATR-Chk1-p53 [39] pathway, where the damage recognition proteins activate ATR kinase, which phosphorylates Chk1 kinase. The protein p53 is then activated subsequently and can induce apoptosis [40]. p53 is a sequence-specific transcription factor and tumor suppressor. It activates the downstream apoptosis pathway leading to tumour cell death [41].

Apoptosis might be a result of the disruption of nuclear and mitochondrial DNA structure[42]. Mitochondria are small organelles involved in oxygen and energy metabolism in the cell and contain their own self-replicating DNA that encodes important proteins for oxidative phosphorylation [43]. Since platinating agents have the strong ability to bind to mitochondrial DNA as well, mitochondria and oxidative pathways become susceptible to their toxicity. Through attacking mitochondrial DNA, platinating agents can trigger an excessive production of reactive oxygen species (ROS) by the catalytic effect of NADPH oxidases whose function is to

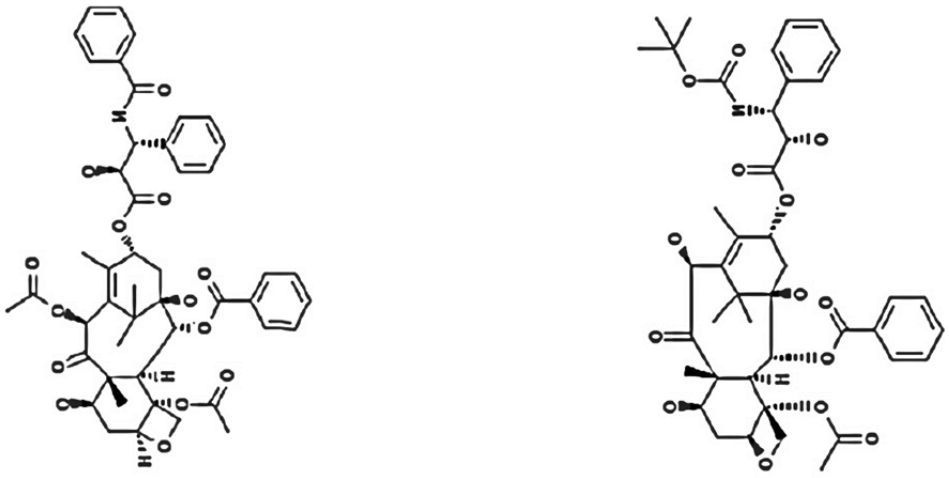
transport electrons across the mitochondrial membrane and to generate ROS [44,45]. Through a series of cell signaling pathways, elevated levels of ROS can also lead to p53 activation[46,47]. Cisplatin attacks on mitochondria also result in depletion of glutathione (GSH), calcium uptake inhibition and reduction of mitochondrial membrane potential [48].

p53 transcriptionally regulates many apoptosis-related genes [41,49]. Bcl-2 (B-cell lymphoma 2), Bcl-X_L (B-cell lymphoma-extra large), Bax (Bcl-2-associated X protein) are members of the Bcl-2 family and are apoptosis regulator proteins [50]. p53 promotes the level of BAX gene transcription [51] as well as the binding of pro-apoptotic Bax to a mitochondrial voltage-dependent anion channel (VDAC). The binding increases cytochrome c release from the mitochondria [52,53]. Through the interaction between cytochrome c and Apaf-1 (Apoptotic protease activating factor 1), a cascade of caspases are activated by phosphorylation, which leads to apoptosis [54]. On the other hand, p53 transcriptionally down-regulates the expression of anti-apoptotic proteins Bcl-X_L and Bcl-2 [55].

Cisplatin is still considered to be the most potent among the platinum-based anti-cancer agents in spite of its strong nephrotoxicity, which was a big concern for this first generation platinating agent. Its derivatives such as carboplatin and satraplatin are used as the mainline treatment of ovarian cancer as well. Carboplatin has a lower excretion rate, meaning its effects are longer lasting [56]. Compared to cisplatin, carboplatin is less nephrotoxic, which is considered to be its greatest benefit. Cisplatin breaks down to unstable hydrolysis products which are rapidly bound to plasma proteins and extensively filtered, with some active secretion by the kidney. This high renal concentration is thought to be the major cause of nephrotoxicity. Carboplatin may be less nephrotoxic than cisplatin because carboplatin is more soluble and chemically stable and binds more slowly to plasma proteins [57,58].

1.2.2 Taxanes and Cytotoxicity

In the 1960's, a natural compound was extracted from the bark of *Taxen brevifolia*, the Pacific Yew Tree, and was named Taxol (paclitaxel). Paclitaxel is highly lipophilic and consists of an eight-member taxane ring with a four-member oxatane ring and an ester side chain that is necessary for antitumour activity [59]. It has been used mostly in the treatment of breast, ovarian, prostate, and non-small cell lung cancer [60]. A semisynthetic form of the drug, docetaxel or Taxotere was developed and is currently widely used clinically [61].



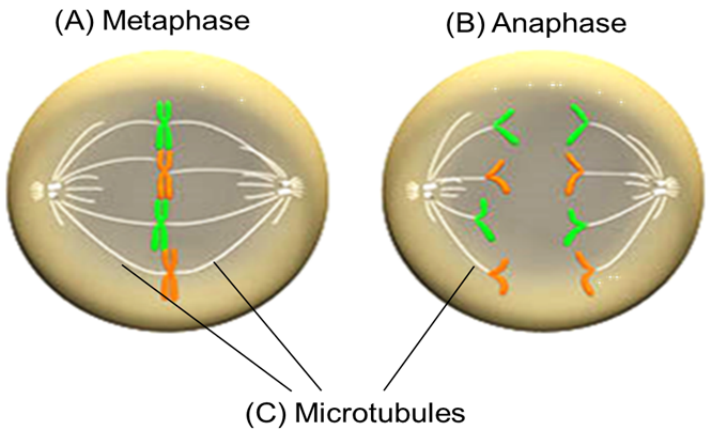
(A) (B)

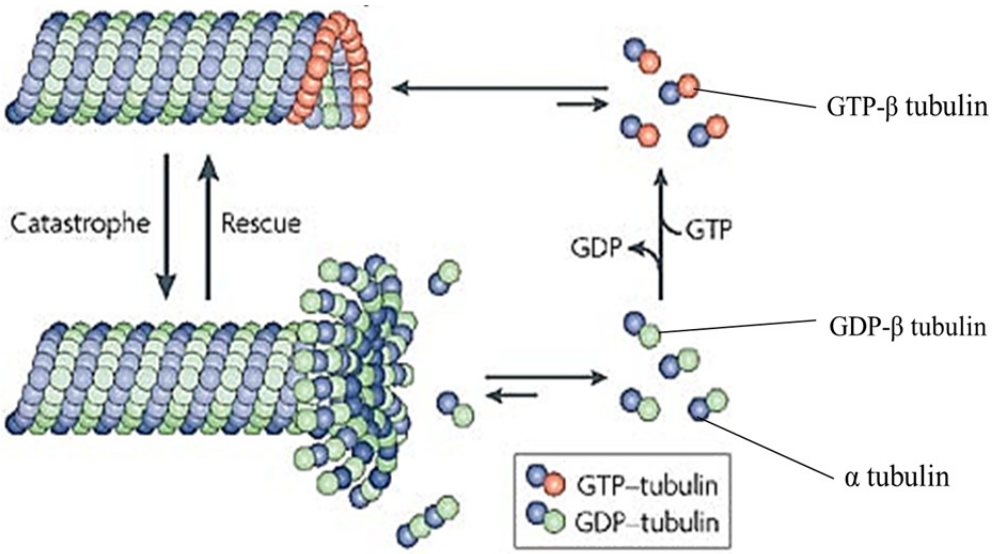
Figure 1.3 Chemical structure of taxanes.

Chemical structures of (A) Paclitaxel and (B) Docetaxel (taken from reference 61).

During cell proliferation, metaphase occurs when condensed chromosomes line up at the equatorial plate within cells. The chromosomes are attached by microtubules stretched from two poles of the cells, which facilitate chromosome segregation equally between two daughter cells [62]. These microtubules are the targets of taxanes. To be more precise, taxanes bind to β-tubulin

subunits of microtubules to manifest their function [63,64]. Most commonly, the cytotoxicity of taxanes is a result of the binding of drug to microtubules. It has been known that taxanes accelerate microtubule polymerization, without permitting depolymerisation that normally follows [65].





(D) Polymerization (Rescue) and depolymerisation (Catastrophe) of microtubules

Figure 1.4 Mitosis and microtubules

(A) metaphase, (B) anaphase, and (C) microtubules (taken from reference 66); (D) The micro-structure of microtubules and their dynamics: polymerization (rescue) and depolymerisation (catastrophe) (taken from reference 67).

The consequent arrest of the cell cycle at mitotic phase has been considered to be the initial cause of paclitaxel-induced cytotoxicity [68,69]. For example, when microtubules are stabilized, it activates JNK/SAPKs (c-Jun N-terminal kinases/stress-activated protein kinases) and promotes apoptosis[70]. The mitotic arrest also causes phosphorylation of Bcl-2, inhibiting its anti-apoptotic effect [71,72]. Moreover, studies have shown that after the mitotic spindle is stabilized, the cell enters a multinucleated state. The downstream events are not clear now, but activation of p53 is observed, which leads to subsequent apoptosis [73,74].

Paclitaxel can also directly initiate apoptosis in cells at the transcriptional level. High concentrations of paclitaxel can induce an up-regulation of pro-apoptotic Bax and a down-regulation of anti-apoptotic Bcl-X_L [75]. This then promotes apoptosis through the induction of cytochrome c release, binding to Apaf-1, and caspase-3 activation.

Taxanes are metabolized by cytochrome P450 (CYP450) enzymes mainly in the liver [76]. There are studies showing the pharmacokinetics of taxanes, where CYP3A catalyzes oxidation of paclitaxel, forming 6-alpha-hydroxypaclitaxel which is an inactive form of the drug [77,78]. The choice of use between paclitaxel and docetaxel varies. There is some evidence that docetaxel is more potent at killing cancer cells than paclitaxel, since the former has a longer retention time due to its greater uptake and reduced efflux from tumour cells [79]. However, docetaxel can often have more severe side effects than paclitaxel, mainly due to its ability to induce strong neutropenia (low white blood cell count). This, however, can be effectively managed by using pegfilgrastim to stimulate new white blood cell growth [80,81]. All in all, the choice between paclitaxel and docetaxel depends on multiple factors such as the treatment regimen, the type of cancer, and the health of patients [82].

1.2.3 Combination of Platinating Agents and Taxanes

Combining platinating agents and taxanes has become the standard of care for the treatment of ovarian cancer patients. In comparing single agent therapy to combination therapy, the overall survival rate was much higher in the latter case. Parmar *et al*. [83] randomized patients into platinum-based and platinum/paclitaxel-based arms in 2003. The results showed that progression-free survival in the former arm was 9 months, while in the latter arm, it was significantly longer (12 months; p=0.06). Nevertheless, such short progression-free survival times for both regimens underscores the need for more effective chemotherapy or other treatment methods for ovarian cancer patients. The administration of these anticancer agents is usually through intravenous (*i.v.*) infusion or intraperitoneal (*i.p.*) injection [84]. In 1996, 410 patients with debulked stage III or IV tumours were randomized into two groups receiving either cisplatin/cyclophosphamide or cisplatin/paclitaxel chemotherapy. Results showed that progression-free survival at 18 vs 13 months was significantly higher in the cisplatin/paclitaxel group (18 months) than cisplatin/cyclophosphamide group (13 months) ($P = 0.01$). Overall survival duration was also significantly longer in patients treated with cisplatin/paclitaxel (38 months vs 24 months, $P < 0.001$) [18]. As it became evident that carboplatin is equally effective with less organ toxicity than cisplatin, carboplatin took over as standard of care for the treatment of ovarian cancer (along with paclitaxel or docetaxel) [85]. The concept of combining platinum-based agents and taxanes was to let patients undergo administration of both to exert a strong synergetic effect before acquisition of resistance to either drug. A typical infusion scheme of carboplatin/paclitaxel is once every three weeks for 6 to 9 cycles. Recent "dose dense" regimens using weekly paclitaxel administration with tri-weekly carboplatin yield a better response rate [86]. Progression-free survival was 28 months for the dose-dense regimen compared to 17.2 months

for the standard regimen. The overall survival rate was respectively 72.1% and 65.1% in three years, respectively [86]. Clinician scientists have also tried to add a third anti-cancer agent to the regimen, but this did not show better outcomes [87]. This indicates that the carboplatin/taxane combination remains the most effective chemotherapy regimen to date for the treatment of ovarian cancer. Among the cancer patients treated with a combination of platinating agents and taxanes, 70% will respond to the regimen. However, even with combination chemotherapy, the majority of the patients that respond will experience disease recurrence, at which time the tumour acquires strong resistance to both platinating agents and taxanes [88]. This situation calls for both the development of new anti-cancer agents and/or improved approaches to combat acquired resistance to platinating agents and taxanes.

1.3 Mechanisms of Resistance

1.3.1 Innate vs. Acquired Resistance

In the beginning of treatment for ovarian cancer, approximately 30% of patients do not respond to adjuvant chemotherapy. These patients are said to have innate resistance, despite the lack of prior exposure to chemotherapy agents. While the remainder respond to treatment, the tumours of such patients eventually become drug resistant [89]. In this situation, the cells of recurrent tumours are said to have acquired drug resistance. Both resistance mechanisms remain a major challenge to the successful treatment of ovarian cancer. A better understanding of the mechanisms underlying both innate and acquired resistance may help uncover novel approaches to circumvent these mechanisms.

1.3.2 Resistance *in vitro* vs. *in vivo*

Multiple mechanisms are believed to be responsible for drug resistance at the cellular level, including gene mutations, gene amplifications or changes in the expression or activity of proteins that influence the uptake, efflux, targeting and metabolism of chemotherapy drugs [89–91]. In addition, Reed and *et al.*, and others identified epigenetic changes associated with acquired drug resistance [92–94]. It is very important to note that many of the above mechanisms were identified largely through experiments on cells cultured *in vitro*, meaning outside the living organism. In these studies, cancer cells are placed in a plastic flask and are bathed in medium that contains nutrients and factors to promote cell survival. Thus, in contrast to cells in animals and humans (*in vivo*), cellular pathways promoting survival predominate over pathways promoting cell death under these ideal conditions [95,96]. Thus, to truly understand resistance to chemotherapy agents in cancer patients, studies should not be limited to cell cultures, since tumour cells within the human body form associations with cells of other tissues and vary in terms of their distance from the nearest blood vessel. Cells in the center of a tumour are less exposed to nutrients, oxygen, and chemotherapy drugs than cells near the tumour surface. In the context of ovarian cancer, solid tumours grow in a microenvironment [97] that also includes interactions with and exposure to stromal cells (fibroblasts, immune cells, and inflammatory cells), the tumour vasculature and extracellular matrix (ECM). Compared with normal tissues, tumours have a very different extracellular matrix, usually with an increased number of fibroblasts that synthesize growth factors, chemokines, and adhesion molecules. The diseased tumour stroma can enhance tumour cell expansion and malignant transformation and can reduce the sensitivity of tumour cells to drugs [98–101], which is not seen *in vitro*. Secondly, the higher "packing density" of tumour and stromal cells can hinder the access of drugs to some tumour cells [102], conferring resistance that's not seen in cell culture. Thirdly, the tumour vasculature and the blood flow will affect the solid

tumour microenvironment [103,104]. The morphology of tumour blood vessels is also very different from that of normal tissues [104]. These vessels contain excessive branching, loops and shunts, making blood flow unevenly distributed. The level of nutrients and oxygen can differ within areas of a solid tumour. Without sufficient levels of nutrients and oxygen, tumour cells have a lower proliferation rate, rendering them less sensitive to anti-cancer agents. A hypoxic tumour microenvironment can also lead to the activation of genes associated with angiogenesis and cell survival, and this effect is mediated by the transcription factor hypoxia inducible factor 1 (HIF-1) [105,106]. It is known that hypoxia often selects for cells deficient in DNA mismatch repair, which may help account for resistance to platinating agents in ovarian cancer *in vivo* [107,108]. Lastly, the lymphatic system plays a role in the clearance of metabolites and wastes in the microenvironment [109]. However, the shortage or absence of lymphatic vessel in solid tumours leads to interstitial hypertension in the tumour which impairs the penetration of macromolecules such as taxanes.

1.4 Platinating Agents and Their Mechanisms of Resistance *in vitro* and *in vivo*.

The mechanisms of resistance to platinum-based anti-cancer agents have been widely studied in cultured cells *in vitro*. Mechanisms involve enhanced DNA repair, decreased drug uptake, increased drug efflux and drug detoxification. The interruption of downstream apoptotic pathways has also been implicated in resistance to platinum agents. Firstly, since the target of platinating agents is double-stranded DNA, it is well-understood that a reduction in chemosensitivity may be associated with cellular responses to the DNA damage induced by these agents. Upon the formation of platinum-DNA adducts, cells can remove the adduct through DNA nuclear excision repair (NER) and base excision repair (BER) [110]. Consistent with this view, cisplatin has been shown to be highly effective against testicular carcinoma when tumours

lack sufficient ability to repair platinum-damaged DNA structures [111]. Moreover, the over-expression of DNA polymerase β can promote resistance to tumour cell killing by platinating agents through its ability to promote repair of the DNA damage [112]. Transfection of cells with expression vectors containing cDNA that is coded for a DNA polymerase β cDNA have been shown to induce cisplatin resistance [113]. Resistance to platinating agents can also arise when drug uptake or accumulation is decreased. Uptake of platinating agents in tumour cells depends mainly upon the activity of the cell surface copper transporter 1 (CTR1) [114]. CTR1 is able to actively transport copper ions and cisplatin into the cytoplasm and CTR1-deficient tumour cells demonstrate resistance to cisplatin [115]. Cisplatin was shown to cause CTR1 internalization. This internalization results in reduced uptake of the drug and cisplatin resistance [116]. Thirdly, an increase in efflux of platinating agents from cells or from the nucleus into the cytoplasm also accounts for reduction in drug efficacy. For example, the copper-transporting P-type adenosine triphosphatases ATP7A and ATP7B were found to efflux both cisplatin and carboplatin from cells [117,118]. When an ATP7B cDNA expression vector was transfected into human epidermoid carcinoma KB-3-1 cells, the transfected cells were found to be resistant to both cisplatin (8.9-fold) and copper (2.0-fold) [119]. Evidence of clinical relevance for ATP7B in tumour resistance to cisplatin in cancer patients was provided in a recent study showing that ATP7B overexpression is associated with poor outcome in cisplatin-treated patients with esophageal cancers and squamous cell cancers of head and neck [120,121].

Upon platinating agents entering tumour cells, cellular glutathione can bind and inactivate the drugs. Glutathione (GSH) is a tri-peptide (Glu-Cys-Gly) [122] that binds to platinating agents and serves as a co-factor to facilitate drug export from tumour cells, thereby conferring resistance to platinating agents [123,124]. In addition, Glutathione-*S*-transferase (GST) augments platinating agent

resistance by catalyzing the formation of covalent bonds between GSH and platinating agents. GST gene amplification or GST immunostaining in tumoursand plasma correlated with cisplatin resistance in patients with cancers of the head and neck [125–127], suggesting that drug detoxification or transport by GSH and/or GST may play a role in clinical resistance to platinating agents. GSH can also confer resistance to cisplatin by enhancing DNA repair, or reducing cisplatin-induced oxidative stress [128]. Lastly, cisplatin resistance has also been associated with blockage of drug-induced apoptosis through mechanisms such as mutations in p53 [129] and decreased expression of the death receptor Fas [130]. The overexpression of the apoptotic inhibitors Bcl-2 or Bcl-X_L overexpression has also been found to be associated with cisplatin resistance and reduced disease-free survival in ovarian cancer cell lines [131]. The apoptotic caspases 3 and 8 were also found to be downregulated in ovarian cancer cells exhibiting cisplatin resistance [132]. Since tumour cells in patients are adjacent to stromal cells, the chemical components in interstitial fluid become very complex. Binding of drug to proteins in the interstitium can also contribute to resistance by binding cisplatin and reducing drug uptake into tumours [133].

1.5 Taxanes and Their Mechanisms of Resistance *in vitro* and *in vivo*.

In vitro studies have identified several mechanisms of resistance to taxanes. They are mainly associated with increased drug efflux by members of the ABC (ATP binding cassette) transporter family. Other mechanisms involve altered expression of tubulin subunits (or mutations in the genes coding for these subunits), as well as changes in the activity or expression of apoptotic regulatory proteins. *In vivo*, the upregulation of taxane metabolizing agents from the cytochrome P450 family in liver was also observed to confer taxane resistance.

One or more members of the large family of ABC transporters exist on the membranes of all human cells. They function as efflux pumps that can transport structurally diverse, lipophilic compounds, including taxanes, out of the cell. The best known member of this family is P-gp (p-glycoprotein, Abcb1) which is encoded by the *ABCB1/MDR1* gene [134]. The overexpression of Abcb1 in tumour cells leads to decreased accumulation of taxanes and, hence, drug resistance [135]. Many *in vitro* studies have shown an inverse correlation of *MDR1* gene expression with cellular sensitivity to paclitaxel, with confirmation of increased *MDR1* mRNA and P-gp protein expression in paclitaxel-resistant cell lines [136,137]. Another major mechanism of resistance to taxanes *in vitro* involves mutations in genes that code for tubulins, the binding targets for taxanes. Paclitaxel-resistant ovarian cancer cell lines showed point mutations in type I β-tubulin, which cause conformational changes in tubulins and the dynamics of microtubule polymerization /depolymerisation [138,139]. A unique mechanism of taxane resistance involves enzymes that are able to metabolize the drug and convert it into less toxic derivatives [140,141]. Enzymes from the cytochrome P450 family have been implicated in taxane resistance [142,143]. A marked increase in resistance to docetaxel was observed in Chinese hamster ovary cells that expressed the *CYP1B1* gene in higher amounts than parental cells [142]. A clinical study by McFadyen *et al*. [143] noted increased expression of *CYP1B1* in primary and metastatic ovarian tumours, compared to normal ovary tissue.

1.6 Cell lines for *in vitro* study of ovarian cancer

When studying the function and mechanism of action of chemotherapeutic agents for ovarian cancer, cell lines are the most basic materials to start with. The ovary is made up of three different kinds of cells, each of which can develop into a different type of tumour, originating from epithelial cells, germ cells or stromal tissue [144]. Some ovarian malignancies can also be a

result of the metastasis of fallopian tube cancer [145]. Among these different cancer cells from different origins, the most common type of ovarian cancer is epithelial in origin. Furthermore, epithelial ovarian cancer (EOC) can be divided into high-grade serous, low-grade serous, clear cell, endometrioid, and mucinous, each of which might have a different response rate in clinical settings [146]. In this complicated context, biomarker identification and validation may be dependent upon the specific cell line(s) used in experiments. The parental A2780 human ovarian cancer cell line was derived from an ovarian cancer patient prior to chemotherapy treatment [147]. Therefore, it is a chemotherapy-naïve cell line and has epithelial morphology [148]. Approximately 90% of all ovarian cancers develop from the epithelium of the ovary and thus the A2780 cell line is appropriate for the goals of this investigation [149]. The parental cell line A2780 was used previously by our research group to generate a carboplatin-resistant A2780 cell line ($A2780_{CBN}$) and a docetaxel-resistant cell line ($A2780_{DXL}$) [150].

These cells grow as a monolayer *in vitro* as in epithelia but are likely of endometrioid subtype [151]. In addition to SK-OV-3, CaOV3, and OVCAR-3 cell lines, A2780 cells are widely used in the study of ovarian cancer *in vitro* [151]. Although A2780 cells have a deficiency in the DNA mismatch repair pathway, have wild-type TP53, and other mutations uncharacteristic of High Grade Serous Ovarian Cancer (HGSOC) [148], they still have strong advantages because many mature models for the study of ovarian cancer were established using A2780 cells. Moreover, its resistant sublines are very stable.

1.7 Study Design, Aims and Hypotheses

The treatment of ovarian cancer has been improving slowly in clinical settings. With the established effect of platinating agents, taxanes, and a combination of the two, the way the

regimen is administered becomes important. Previously, *in vitro* studies have established and characterized ovarian cell lines resistant to single agents (carboplatin or docetaxel) or to dual agents (namely carboplatin and docetaxel) [150]. It was found that the above single agent resistant cell lines exhibited an inverse relationship between resistance to taxanes and resistance to platinum-based agents (and vice versa) [150,152,153], suggesting that there is little cross resistance between these agents *in vitro*. On the clinical side, longer time intervals between treatments have been shown to affect patient response to chemotherapy and alternating treatment with different drugs has shown promise in avoiding or overcoming resistance [154–158]. Both these observations may indicate that genetic changes resulting in improved response to chemotherapy are time and dose dependent, as well as affected by the drug in use. Therefore, we planned an approach to study these effects *in vitro* using the single agent resistant cell lines, $A2780_{CBN}$ cells (resistant to carboplatin) and $A2780_{DXL}$ cells (resistant to docetaxel). By culturing the $A2780_{CBN}$ and $A2780_{DXL}$ cell lines in the absence of drug, we can investigate the ability of the resistance to persist over time and the changes in gene expression that may occur if primary resistance reverts to sensitivity. By culturing the $A2780_{CBN}$ cell line in increasing doses of docetaxel and the $A2780_{DXL}$ line in increasing doses of carboplatin, we can investigate the ability of a primary resistance to persist in the presence of another drug, allowing us to study how a primary resistance may change if exposed to an alternate drug. In addition, the development of resistance to the secondary drug may be studied. *We hypothesize that after sufficient exposure to one drug in this combination (until resistance is obtained), exposure to the other drug for several cycles of treatment may re-sensitize cells to the previously administered drug at a faster rate than simply leaving cells drug-free for an equivalent period of time.* In other words, exposure of carboplatin-

resistant cells to docetaxel and selection for docetaxel resistance may result in re-establishment of carboplatin sensitivity and vice versa.

In order to test this hypothesis, the objectives of this thesis were:

Aim (1): to select carboplatin-resistant cells for resistance to docetaxel *in vitro* to generate $A2780_{CBN \rightarrow DXL}$ cells;

Aim (2): to select docetaxel-resistant cells for resistance to carboplatin *in vitro* to generate $A2780_{DXL \rightarrow CBN}$ cells; and

Aim (3): to assess the effect of new drug resistance on prior drug resistance.

After patients have received chemotherapy treatment, they often receive no further chemotherapy treatment for an extended period of time. This is called the "drug-free interval" and this may also play a role in restoration of chemotherapy sensitivity (as suggested in prior clinical studies). Consistent with this view, it was found that the longer time interval between chemotherapy after recurrence of ovarian cancer, the better response is in later treatment [159]. This evidence suggests that sensitivity to a previously administered drug may be restored by simply removing exposure to the drug. To assess the role of the drug-free interval on restoration of chemosensitivity, we also planned:

Aim (4): to assess the effect of withdrawal of selection pressure for carboplatin-resistant cells ($A2780_{CBN \rightarrow CC}$ cells) on their sensitivity to paclitaxel and docetaxel, and

Aim (5): to assess the effect of withdrawal of selection pressure for docetaxel-resistant cells ($A2780_{DXL \rightarrow CC}$ cells) on their sensitivity to paclitaxel and docetaxel.

We thus further hypothesize that restoration of drug sensitivity will occur more rapidly upon selection/exposure to a new drug than by simply stopping exposure to the previously administered drug.

It would also be helpful to identify changes in gene or protein expression that accompany restoration of sensitivity to the previously administered drug and acquisition of resistance to a new agent. This could provide significant insight into the mechanisms responsible for restoration of sensitivity to the previously administered drug and/or the mechanisms for acquisition of resistance to the new agent. By profiling gene expression in the above newly established cell lines and comparing with previous profiling studies, we also planned:

Aim (6): to identify changes in gene expression associated with the loss and gain of drug resistance in the newly established cell lines.

To further clarify our expectations, we hypothesize that in a comparison of the docetaxel-resistant cell line that was previously carboplatin-resistant ($A2780_{CBN\rightarrow DXL}$) with the carboplatin resistant cell line ($A2780_{CBN}$), the gene expression changes will be associated with both the loss of carboplatin resistance and the gain of docetaxel resistance. The same would apply for the comparison between the carboplatin-resistant cell that was previously resistant to docetaxel ($A2780_{DXL\rightarrow CBN}$) and the docetaxel resistant cell line ($A2780_{DXL}$). Secondly, by comparing the cell line representing removal of $A2780_{CBN}$ cells from carboplatin selective pressure ($A2780_{CBN\rightarrow CC}$) with the carboplatin-resistant cell line ($A2780_{CBN}$), the resulting changes in gene expression may be associated with the loss of carboplatin resistance during the drug-free interval, if carboplatin resistance is lost. Similarly, by comparing the cell line representing removal of docetaxel selective pressure ($A2780_{DXL\rightarrow CC}$) with the docetaxel resistant cell line ($A2780_{DXL}$), the

changes in genes expression may be associated with loss of docetaxel resistance, if this phenotype is also lost. Thirdly, by studying the common and unique gene expression changes associated with the above comparisons, we should be able to identify common or unique genes, whose expression is altered upon restoration of drug sensitivity, whether it is by exposure to a new agent or by withdrawal of an existing agent. These gene profiling studies should provide us with important insight into possible mechanisms that could be exploited to restore chemosensitivity to chemoresistant tumours in ovarian cancer patients.

Chapter 2

2. Materials and Methods

2.1 Cell Lines and Culture

The human A2780 ovarian carcinoma cell line was purchased from the European Collection of Authenticated Cell Cultures (ECACC, Salisbury, UK) and maintained in drug-free cell growth medium (RPMI-1640 with 2 mM glutamine supplemented with 10% FBS, 100 U penicillin, and 0.1 mg/ mL streptomycin, all obtained from HyClone, South Logan, Utah, USA). The cells were incubated in 10 mL of the above medium in T75 flasks with vented cap (SARSTEDT, Montreal, QC). The flasks were placed in a humidified incubator at 37^{o}C with 5% CO2. The cells were initially plated at a confluence of 30-40%. The medium was changed every 48 hrs until cells reached a confluence of 70-80%. When the cells reached confluence, subculturing was performed by adding 0.05% trypsin/EDTA solution (HyClone, South Logan, Utah, US) to the cells. Chemoresistant $A2780_{CBN}$ and $A2780_{DXL}$ cell lines were provided by Dr. Carita Lanner of the Northern Ontario School of Medicine (Sudbury, Canada). The resistance to carboplatin in the $A2780_{CBN}$ cell line was maintained by adding 22.2 μM of the drug in RPMI-1640 with 2 mM glutamine, 10% FBS and penicillin/streptomycin. Likewise, the resistance to docetaxel in the $A2780_{DXL}$ cell line was maintained by adding 0.405 μM docetaxel in RPMI-1640 with 2 mM glutamine, 10% FBS and 1% penicillin/streptomycin. The resistance to docetaxel in a cell line where $A2780_{CBN}$ cells were selected for resistance to docetaxel ($A2780_{CBN\rightarrow DXL}$ cells) was maintained by adding 1.09 nM docetaxel in RPMI-1640 with 2 mM glutamine, 10% FBS and penicillin/streptomycin. The resistance to carboplatin in a cell line where $A2780_{DXL}$ cells were

selected for resistance to carboplatin ($A2780_{DXL \rightarrow CBN}$ cells) was maintained by adding 8.20 μM carboplatin in RPMI-1640 with 2 mM glutamine, 10% FBS and penicillin/streptomycin. The medium containing drug was changed every 48 hrs.

2.2 Cell Line Selection

$A2780_{CBN \rightarrow DXL}$ cells were generated from $A2780_{CBN}$ cells through selection in increasing concentrations of docetaxel. The selection started at 1.0 pM docetaxel, which is about 350-fold below the average IC_{50} value for docetaxel in $A2780_{CBN}$ cells (0.36 nM ± 0.31 pM) [150] and was denoted as Selection Dose 1 (S1). Similarly, $A2780_{DXL \rightarrow CBN}$ cells were generated using $A2780_{DXL}$ cells, through selection in increasing concentrations of carboplatin with an S1 dose of 1.0 nM carboplatin, which is about 2200-fold below the average IC_{50} value for carboplatin in $A2780_{DXL}$ cells (2.20 μM ± 0.33μM)[150].

The starting dose of carboplatin (1.0 nM) is higher than that of docetaxel (1.0 p M), because in previous experiments by Armstrong, *et al* [150], the IC_{50} of carboplatin in $A2780_{DXL}$ cells are higher than that of docetaxel in $A2780_{CBN}$ cell, meaning carboplatin is less toxic to cells than docetaxel.

Fresh medium containing drug at S1 was replaced every 48 hrs. When confluence reached 70-80%, the cells would undergo sub-culturing. Twenty four hrs after sub-culturing, the medium containing the same dose of respective drug was added to the cells. After reaching 70-80% confluence, the cells were trypsinized and lifted from the bottom of the flask. Aliquots of the cells for cryostorage were maintained at a density of approximately 1 million cells/ mL in a medium that contained 20% FBS and 5%-10% DMSO. They were transferred to 1mL cryovials and stored in liquid nitrogen. The rest of the cells were re-plated in new flasks. After 24 hrs to

allow cells to attach to the bottom of the flask, medium containing higher concentrations of drug was added to various flasks of the cells. These had drug concentrations 1.25-fold, 1.5-fold, or 3-fold higher than S1. Cells surviving in the highest of these drug concentrations were transferred into new flasks and aliquots were stored in liquid nitrogen. The highest concentration of drug in which cells survived was denoted as Selection Dose 2 (S2). This entire selection procedure was repeated until $A2780_{CBN \rightarrow DXL}$ cells reached S8 and $A2780_{DXL \rightarrow CBN}$ cells reached S10 since cells could not survive in the dose. A co-cultured control (CC) cell line was also prepared ($A2780_{CBN \rightarrow CC}$ cells) by culturing $A2780_{CBN}$ cells in the absence of docetaxel for the same number of passages as the $A2780_{CBN \rightarrow DXL}$ cell line in the same incubator as the drug-selected cells. These were also stored in liquid nitrogen. Similarly, co-cultured $A2780_{DXL \rightarrow CC}$ cells were generated by culturing $A2780_{DXL}$ cells in the absence of carboplatin for the same number of passages as the $A2780_{DXL \rightarrow CBN}$ cell line. The chemotherapy naïve A2780 cell line was cultured in drug free medium ($A2780_{CC}$ cells) as a control for changes in drug sensitivity or gene expression due to multiple passages of continuous cell culture.

2.3 Cell Viability Test

2.3.1 Preparation of Methylcellulose

In order to suspend the cells in a medium that allows them to form countable colonies in 3 dimensions, a solution of methylcellulose was used. An Erlenmeyer flask containing a magnetic stirring bar was autoclaved on a minimum 20 min gravity cycle and then weighed. Four hundred and sixty (460) mL of sterile Baxter water was added to the flask and brought to a boil. Fifteen grams of methylcellulose powder (Sigma Aldrich, St Louis MO USA) was added to the flask which was shaken vigorously for 7-8 min to evenly suspend the powder. Subsequently, a volume

of 500 mL of Iscove's Modified Dulbecco's Medium (IMDM) with 1% penicillin/streptomycin (HyClone, South Logan, Utah, US) was added to the methylcellulose mixture in a tissue culture hood. The mixture was stirred at 4°C overnight and became clear and extremely viscous. On the second day, 70 mL aliquots of the uniform methylcellulose solution were placed into 100 mL of sterile urine specimen cups and were frozen at -20°C.

2.3.2 Clonogenic Assays

$A2780_{CBN \rightarrow DXL}$, $A2780_{DXL \rightarrow CBN}$, $A2780_{CBN \rightarrow CC}$, $A2780_{DXL \rightarrow CC}$, $A2780_{CBN}$, $A2780_{DXL}$, $A2780_{CC}$ were assessed for their sensitivity to either carboplatin or docetaxel using standard clonogenic assays. Each of the cell lines was allowed to reach 70-80% confluence. Then the cells were lifted from a T75 flask by trypsin/EDTA treatment and plated in 12 T25 flasks with each flask containing the same number of cells (0.2×10^6 cells per flask). The cells were placed in 5 mL of drug-free RPMI-1640 medium containing 2 mM glutamine, 10% FBS and 1% penicillin/streptomycin. After 24 hrs, the medium was removed from each flask and replaced with fresh medium containing different concentrations of docetaxel or carboplatin. The 12 flasks were numbered 1 to 12, with 1 containing the highest concentration of the drug and 12 lowest as no-drug control (docetaxel doses 1 to 11: 100 μM, 0.1 μM, 10 nM, 3 nM, nM, 0.3 nM, 0.1 nM, 30 pM, 10 pM, 1 pM, 0.1pM. Carboplatin doses 1 to 11: 1 mM, 0.1 mM, 30 μM, 10 μM, 3 μM, 1 μM, 0.3 μM, 0.1 μM, 30 nM, 10 nM, 1 nM). After 24 hrs, 30 mL of FBS were added to a thawed, stored 70 mL aliquot of methylcellulose and the sample shaken vigorously until the mixture became uniform. After allowing the bubbles to vent by gravity, 2.7 mL aliquots of the methylcellulose mixture were placed into 13 mL Rohre tubes. After 24 hrs of incubation in the absence or presence of drug, the medium in the T25 flasks was removed and transferred to

individual 15 mL tubes. The cells in each T25 flask were released with 1 mL of trypsin/EDTA solution and transferred to the correspondingly labeled tube. Each flask was washed once with 2 mL of PBS (HyClone, South Logan, Utah, USA) to ensure all viable cells were collected. The cells were centrifuged at 1000 rpm for 8 min. The supernatant was discarded and 300 μL fresh medium was added to suspend the cell pellet. The whole suspension was pipetted into corresponding labeled Rohre tubes containing 2.7 mL of methylcellulose solution. The mixtures containing cells were vortexed thoroughly to ensure even distribution of this cell-methylcellulose suspension, 1.2 ml were placed into one correspondingly labeled well in a 6-well plate (2 x 6 well plates per clonogenic assay). Each well was numbered 1-12 to represent the 12 drug concentrations. The plates were incubated at 37^{o}C with 5% CO_2 for 5-7 days until large colonies (>50 cells) were formed and could be counted.

2.3.3 Survival Curves and Average of IC_{50}

After colony formation, the mean number of colonies present in five random microscopic fields was determined for each well (magnification 10x10). Pictures of five random fields (x 10) were taken for manual counting later. The mean number of colonies at a particular drug concentration was divided by the mean number of colonies for the no-drug control to determine the survival fraction. The data were entered into Graph Pad Prism software (Graph Pad Software Inc, La Jolla, CA). The survival fraction was plotted against the log of drug concentration (M). The survival analysis curve log [inhibitor] vs. normalized response – variable slope was used to fit the data and calculate the IC_{50}, where the log [inhibitor] represented the log of the drug concentration, the normalized response represented the survival fraction, and the variable slope allowed for the calculated curve to best fit the data. The drug concentration at which the numbers of colonies was 50% of the no drug control was then computed as the IC_{50} value.

2.3.4 Statistical Determination of IC_{50} Significance

Each experiment was performed three times. Statistical analyses were performed to evaluate the significance of differences in IC_{50} values between different cell lines. A Student's T Test with two-tailed distribution and two-sample equal variance was used as the test for significance. A p value of <0.05 indicates a significant difference between the values of two sets of data.

2.4 Microarray Analysis

2.4.1 RNA Isolation

In order to assess gene expression differences between the cell lines, RNA must be isolated from the various cell lines and its quantity and quality assessed. Total RNA was purified from $A2780_{CBN \rightarrow DXL}$, $A2780_{DXL \rightarrow CBN}$, $A2780_{CBN \rightarrow CC}$, $A2780_{DXL \rightarrow CC}$, $A2780_{CBN}$, $A2780_{DXL}$, and $A2780_{CC}$ cells using Qiagen RNeasy^{TM} Mini Kits (Mississauga, ON, Canada). An amount of 0.5 x 10^6 cells was plated in each of three 3 cm plates with 5mL growth medium. After 24 hr incubation, the cell-culture medium was completely aspirated and the cells washed by adding 500 µL PBS. Subsequently, 350 µL lysis buffer RLT (denaturing guanidine-thiocyanate buffer) was added to the monolayer of cells, and after 1 minute, the lysate was scraped down and pipetted into a 2 mL tube. The lysate was passed 5 times through a 20-gauge needle with a 1 mL syringe, after which 350 mL of anhydrous alcohol was added, with the mixture being pipetted up and down several times. Each sample was then loaded onto an RNeasy spin column and placed into a 2 mL collection tube. The sample was then centrifuged at 10,000 rpm for 30 s to bind the RNA to the spin column. After discarding the flow-through, 700 mL of buffer RW1 was added to each column and then the whole assembly was centrifuged again at 10,000 rpm for 30 s. After discarding the flow-through, 700 µL of buffer RPE was added to each column and the

centrifugation repeated. Another 700 µL buffer RPE was added and the process repeated again. The column was placed into a 1.5 mL sterile collection tube and 50 µL of RNase-free water was added to the membrane in the column to elute bound RNA. The sample was then centrifuged at full speed (14,000 rpm) for 1 min. The eluate was pipetted back on to the column and the process repeated again to ensure complete RNA elution. Aliquots of 5 µL RNA sample were transferred to another sterile tube. The tubes containing RNA samples were stored in -80°C freezer for further use.

2.4.2 Quantity and Integrity of Total RNA

Sufficient quantity and integrity of RNA are essential for microarray analysis and these were assessed using an Agilent 2100 Bioanalyzer (Agilent Technologies, Inc., Santa Clara, CA, USA). One µl of each RNA sample was loaded onto RNA Nano chips after chip priming (Caliper Technologies, Hopkinton, MA, USA). The Agilent bioanalyzer generated a gel-like image of each total RNA preparation, determined the RNA concentration, and quantified RNA integrity as an RNA Integrity Number (RIN). The RIN can range from 1 to 10, where 1 represents totally degraded RNA and 10 is highly intact RNA. The RIN value was calculated by the Agilent Bioanalyzer using a specific algorithm. RIN values of 6.0 or higher were considered of sufficient quality for microarray experiments. Since three RNA samples were prepared per cell line, the quantity and quality of each preparation was determined by running RNA Nano chips on the Bioanalyzer. If all samples met the RNA quality standards, a master solution with an RNA concentration of approximately 100 ng/uL was prepared using all three samples. The master solution was then assessed using the Agilent 2100 Bioanalyzer in order to accurately determine final RNA concentrations and RNA quality.

2.4.3 Preparation of cRNA

After confirmation of sufficient RNA quantity and quality, microarray analysis proceeded, starting with the preparation of cRNA (complementary RNA) using the Agilent Quick Amp Labeling Kit (Santa Clara, CA, USA). Array comparisons included $A2780_{CBN \rightarrow DXL}$ vs. $A2780_{CBN}$, $A2780_{DXL \rightarrow CBN}$ vs. $A2780_{DXL}$, $A2780_{CBN \rightarrow CC}$ vs. $A2780_{CC}$, and $A2780_{DXL \rightarrow CC}$ vs. $A2780_{CC}$. Consequently, RNA was isolated from each of the above cell lines to facilitate these comparisons. Cell lines under comparison were at a similar passage number. To begin array hybridization experiments, Spike A and Spike B solutions were prepared as described by the manufacturer (http://www.agilent.com/cs/library/usermanuals/Public/G4140-90050_GeneExpression _TwoColor_6.9.pdf) [160], where these solutions contained RNA transcripts that anneal to complementary probes on the microarray but not to complementary sequences on the array that represent genes from the human genome. The solutions were used to "spike" the RNA solutions from the cell lines described above, which were first diluted to a concentration of 500 ng RNA in 8.3 µL of sterile distilled water. To the RNA solutions was added 2 µL of Spike A (or Spike B) solution and 1.2 µL T7 Promoter Primer solution. The mixture containing primer and templates was denatured at 65°C, after which a dNTP mixture, DTT, First Strand Buffer, MMLV-RT and RNaseOut were added, as instructed and provided by the manufacturer (Agilent Technologies). By incubating this sample mix at 40°C for 2 hrs and then at 65°C for 15 minutes, cDNA preparations were generated and denatured. In the next step, T7 RNA polymerase was used to generate RNA transcripts of the cDNA (cRNA). During transcription either Cyanine 3-CTP (Cy3, red solution, green fluorescence) or Cyanine 5-CTP (Cy5, blue solution, red fluorescence) were incorporated into the cRNA. Thus, two sets of probes were prepared for array hybridization: one Cy3-labelled cRNA from one cell line and one Cy5-labelled cRNA from the

other cell line. These were then used for comparative assessment of gene expression by array hybridization. In some experiments, the Cy3 and Cy5 dyes were used to label the opposite cRNA preparation in order to control for differences in dye stability or efficiencies in labeling. The reaction mixture was then incubated at 40°C for 2 hours to allow transcription of the cRNAs. Since the 2nd strand cDNA and other reaction components were still present in the mixture, cRNA samples were purified by binding and elution from a Qiagen RNeasy mini spin column. Accordingly, 350 µL of Buffer RLT and 250 µL anhydrous ethanol were added to each cRNA preparation. After thorough mixing, the solution was transferred to a spin column placed in a 2 mL collection tube and centrifuged at 13,000 rpm for 30 s at room temperature. Then, 500µL of Buffer RPE was added to the spin column twice to wash the cRNA and the washes discarded by centrifugation at 13,000 rpm for 30 s at room temperature. To elute the cRNA, 30 µL of RNase-free water was added directly to the column and the column centrifuged at full speed for 30 seconds at 4ºC. The eluate contained the purified cRNA and was kept on ice. The cRNA was quantified using a NanoDrop ND-1000 UV-VIS Spectrophotometer version 3.2.1 (Agilent Technologies). The RNA 260nm/280nm absorbance ratio was recorded as a measurement of RNA purity. An A260/280 ratio of 1.9-2.1 was considered of sufficient purity for microarray analysis. cRNA concentrations (in ng/µL) were measured and used to determine the cRNA yield. A volume that contained 825 ng of cRNA was used for array hybridization, as described below. Cy 3 or Cy5 dye concentrations (pmol/µL) were also recorded to determine the efficiency of dye labelling. Dye labelling efficiency equal to 8.0 pmol of dye/µL of cRNA (or greater) was considered sufficient for array hybridization.

2.4.4 Array Hybridization

The labelled and purified cRNAs were loaded onto 4x44K microarrays (Agilent Technologies) containing oligonucleotides that represent probes for almost the entire human genome. Two identical tubes were prepared, one containing Cy3-labelled cRNA from the first cell line in the comparison and the other containing Cy5-labelled cRNA from the second cell line. Meanwhile, two other tubes were prepared, where one contained Cy5-labelled cRNA from the first cell line and Cy3 labelled cRNA from the second cell line. The four tubes were incubated in fragmentation buffer at 60 ºC for 30 min to fragment the cRNA to increase hybridization efficiency to the oligomer nucleotides on the array. 2x Gex Hybridization Buffer was added to stop the fragmentation and the solutions mixed well without introducing bubbles. The samples were centrifuged at full speed (14,000rpm) for 1 min to drive all the solution off the tube walls and lid. A volume of 100 µL of each mixed sample was loaded into one of the four chambers on a clean array slide. cRNA labelled with C3 dye and cRNA labelled with the Cy5 dye were hybridized to two microarrays, while the reverse-labelled samples were hybridized to the remaining two microarrays to control for differences in dye incorporation or dye quenching between the samples. The slides were placed in a rotisserie within a hybridization oven at 65°C for 17 hrs of hybridization.

2.4.5 Microarray Wash

After hybridization, the slides were immersed and washed in 100% acetonitrile in a staining dish for 5 min. The procedure was repeated once and then acetonitrile was replaced with Milli-Q water for 5 additional washings. The slides were then placed in sufficient Gene Expression Wash Buffer 1 and then Gene Expression Wash Buffer 2 (Agilent Biotechnologies) to avoid ozone-related problems in array scanning.

2.4.6 Array Scanning and "Between-Array" Comparisons

A Gene Pix 4000A Scanner (Agilent Technologies) was used to scan the hybridized and washed array slides. Agilent Feature Extraction software version 9.5.3 (Agilent Technologies, USA) was used to extract gene expression data from the arrays. We extracted genes that exhibited an expression change over 2 fold (upregulated: ≥ 2 fold change, downregulated ≤ -2 fold changes) and at the same time, p was less than 0.05.

The profile of gene expression changes of the following four cell line pairs were directly compared "in array" because the paired samples were loaded on the same chip and the microarray result is "relative" data as a result of comparison:

$A2780_{CBN \rightarrow DXL}$ vs. $A2780_{CBN}$ $A2780_{DXL \rightarrow CBN}$ vs. $A2780_{DXL}$

$A2780_{CBN \rightarrow CC}$ vs. $A2780_{CC}$ $A2780_{DXL \rightarrow CC}$ vs. $A2780_{CC}$

By extracting absolute array data of each cell line in each pair, we were also able to compare gene expression between cell lines that were not loaded and compared directly on array chips. This enabled comparisons in gene expression between the following cell line combinations:

$A2780_{CBN \rightarrow DXL}$ vs. $A2780_{DXL}$ $A2780_{DXL \rightarrow CBN}$ vs. $A2780_{CBN}$

$A2780_{CBN \rightarrow CC}$ vs. $A2780_{CBN}$ $A2780_{DXL \rightarrow CC}$ vs. $A2780_{DXL}$

2.4.7 Identification of Important Changes in Gene Expression

To determine the statistical significance of differences in gene expression changes between the various cell line pairs, SAS software (Statistic analytical software, SAS Institute, US) was used. Common gene expression changes between two sets of comparison and distinct gene expression changes solely in one set of cell lines were noted. For example, certain gene expression changes that happen in $A2780_{CBN \rightarrow DXL}$ vs. $A2780_{CBN}$ were also found in $A2780_{CBN \rightarrow CC}$ vs. $A2780_{CBN}$. On the other hand, it is also of importance to show unique gene expression changes found in $A2780_{CBN \rightarrow DXL}$ vs. $A2780_{CBN}$ but not expressed in $A2780_{CBN \rightarrow CC}$ vs. $A2780_{CBN}$, and vice versa. These comparisons enable differentiation between changes in gene expression due to loss of selection pressure ($A2780_{CBN \rightarrow CC}$ vs. $A2780_{CBN}$) and changes in gene expression due to acquisition of a new drug-resistant phenotype ($A2780_{CBN \rightarrow DXL}$ vs. $A2780_{CBN}$).

Chapter 3

3. Results

3.1 Cell Line Selection and Characterization

3.1.1 Generation of $A2780_{CBN \rightarrow DXL}$, $A2780_{DXL \rightarrow CBN}$, $A2780_{CBN \rightarrow CC}$, $A2780_{DXL \rightarrow CC}$ cell lines

Four new cell lines were established: a carboplatin-resistant cell line that was selected for resistance to docetaxel ($A2780_{CBN \rightarrow DXL}$ cells), a docetaxel-resistant cell line that was selected for resistance to carboplatin ($A2780_{DXL \rightarrow CBN}$ cells), a carboplatin-resistant cell line that was propagated for the same period of time in the absence of any drug ($A2780_{CBN \rightarrow CC}$ cells), and a docetaxel-resistant cell line that was propagated for the same period of time in the absence of drug ($A2780_{DXL \rightarrow CC}$ cells). Multiple clonogenic assays were used to test their sensitivity to either carboplatin or docetaxel or both. In this study, $A2780_{CBN \rightarrow DXL}$ cells, a subline of $A2780_{CBN}$ cells selected for resistance to docetaxel, was generated by treating $A2780_{CBN}$ cells with increasing concentrations of docetaxel. The highest surviving selection dose 8 was 1.09 nM docetaxel after 25 passages (Table 3.1). Likewise, by treating $A2780_{DXL}$ cells with ascending doses of carboplatin, we generated a subline of $A2780_{DXL}$ cells, which was selected for resistance to carboplatin ($A2780_{DXL \rightarrow CBN}$ cells). The cell line reached its maximal selection dose at 8.2 μM carboplatin after 29 passages (Table 3.2).

Table 3.1 $A2780_{CBN \rightarrow DXL}$ selection dose concentrations

Dose number	Treatment dose (docetaxel)	Fold above previous dose
1	1.0 pM	N/A
2	3.0 pM	3.0
3	9.0 pM	3.0
4	27 pM	3.0
5	81 pM	3.0
6	0.24 nM	3.0
7	73 nM	3.0
8*MTD (p25)	1.09 nM	1.5

*MTD=maximally tolerated dose

Table 3.2 $A2780_{DXL \rightarrow CBN}$ selection dose concentrations

Dose number	Treatment dose (carboplatin)	Fold above previous dose
1	1.0 nM	N/A
2	3.0 nM	3.0
3	9.0 nM	3.0
4	27 nM	3.0
5	81 nM	3.0
6	0.24 μM	3.0
7	0.73 μM	3.0
8	2.2 μM	3.0
9	6.6 μM	3.0
10*MTD (p29)	8.2 μM	1.25

*MTD=maximally tolerated dose

We also generated $A2780_{CBN\rightarrow CC}$ and $A2780_{DXL\rightarrow CC}$ cells by growing $A2780_{CBN}$ and $A2780_{DXL}$ in drug-free medium, respectively, for the same number of passages as the above drug-selected cells. As was mentioned earlier, the establishment of $A2780_{CBN\rightarrow CC}$ or $A2780_{DXL\rightarrow CC}$ cells was, firstly, to mimic the drug free interval in the clinical setting. Secondly, these cell lines can serve as a control to determine whether any of the properties of the $A2780_{CBN\rightarrow DXL}$ and $A2780_{DXL\rightarrow CBN}$ cell lines are simply due to removal of carboplatin and docetaxel selection pressure, respectively. Photomicrographs of the resistant sub lines, and their co-cultured control counterparts at similar passage were taken. Comparing the morphology of the new cell lines with those used in the beginning to generate them (Figure 3.1), there appear to be no obvious morphology changes, compared to the original cell lines respectively, in the $A2780_{CBN\rightarrow DXL}$, $A2780_{CBN\rightarrow CC}$, and $A2780_{DXL\rightarrow CC}$ cell lines. However, the $A2780_{DXL\rightarrow CBN}$ subline exhibits a very different morphology from that of $A2780_{DXL}$ cells. These cells were more spindle shaped at the final selection dose (Figure 3.1). This might be a consequence of carboplatin resistance establishmentin $A2780_{DXL}$ cells. However, the $A2780_{CBN}$ cells are not spindled shaped, suggesting that there are clear differences between $A2780_{DXL\rightarrow CBN}$ and $A2780_{CBN}$ cells, despite having acquired resistance to carboplatin.

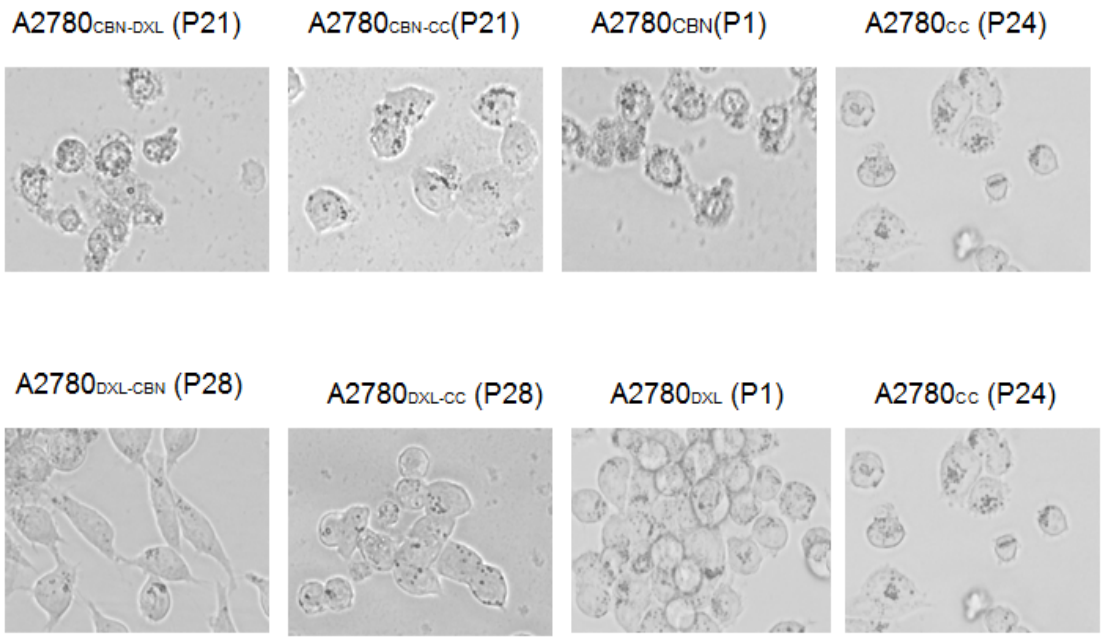


Figure 3.1 Photomicrographs of all resistant cell lines at their final selection doses.

Photomicrographs comparing the cell morphology of the resistant sub cell lines $A2780_{CBN \rightarrow DXL}$, $A2780_{DXL \rightarrow CBN}$, their co-cultured controls $A2780_{CBN \rightarrow CC}$, $A2780_{DXL \rightarrow CC}$, single agent resistant cell lines $A2780_{CBN}$, $A2780_{DXL}$ and parental cell line $A2780_{CC}$ at similar passage numbers. Photomicrographs were taken at 1000x magnification.

3.1.2 Characterization of $A2780_{CBN \rightarrow DXL}$ Cells

To assess the sensitivity of A2780, $A2780_{CBN}$, $A2780_{DXL}$, and $A2780_{CBN \rightarrow DXL}$ cells to docetaxel (Figure 3.2, Table 3.3), these cell lines were incubated with various concentrations of docetaxel ranging from 0.1 pM to 10 μM. The concentration of docetaxel at which colony formation for $A2780_{CBN \rightarrow DXL}$ cells [S8 (selection dose number 8), P25 (passage number 25)] in a clonogenic assay was suppressed by 50% (IC_{50}) was then determined to be 56 ± 9.3 n M, which was 76-fold higher than the IC_{50} for docetaxel in $A2780_{CBN}$ (P1) cells (0.74 ± 0.20 nM, p=0.008). The IC_{50} for docetaxel, however, was 4.2-fold lower than that of $A2780_{DXL}$ (P1) cells (239 ± 59 nM docetaxel p=0.05). This suggests that docetaxel resistance is established in the $A2780_{CBN \rightarrow DXL}$ cell line, but not to the extent seen in $A2780_{DXL}$ cells. While $A2780_{DXL}$ cells were significantly more resistant to docetaxel compared to $A2780_{CBN}$ cells (p=0.005) and A2780 cells (p=0.015), the IC_{50} of $A2780_{CBN}$ cells to docetaxel was not significantly different from that of A2780 cells (p=0.44). In summary, $A2780_{CBN \rightarrow DXL}$ cells exhibited 76 times more resistance to docetaxel than $A2780_{CBN}$ cells, but were 4 times less resistant to docetaxel than $A2780_{DXL}$ cells.

Subsequently, the sensitivity of $A2780_{CBN \rightarrow DXL}$ cells to carboplatin was assessed and compared to that of $A2780_{CBN}$ cells and A2780 cells. (Figure 3.3, Table 3.4). This allowed us to test if prior carboplatin resistance is affected by selection for docetaxel resistance. The cells were treated with carboplatin concentrations ranging from 0.1 nM to 1 mM. The IC_{50} of $A2780_{CBN \rightarrow DXL}$ cells for carboplatin was determined to be 18 ± 6.8 μM. This was not significantly different from the IC_{50} of $A2780_{CBN}$ cells (63 ± 25 μM carboplatin, resistance factor 3.4 fold; p=0.19).

Therefore, the results above indicated that the resistance to docetaxel could be established in $A2780_{CBN}$ cells to obtain an $A2780_{CBN \rightarrow DXL}$ cell line. Moreover, the original resistance to carboplatin was not significantly altered by selection for docetaxel resistance.

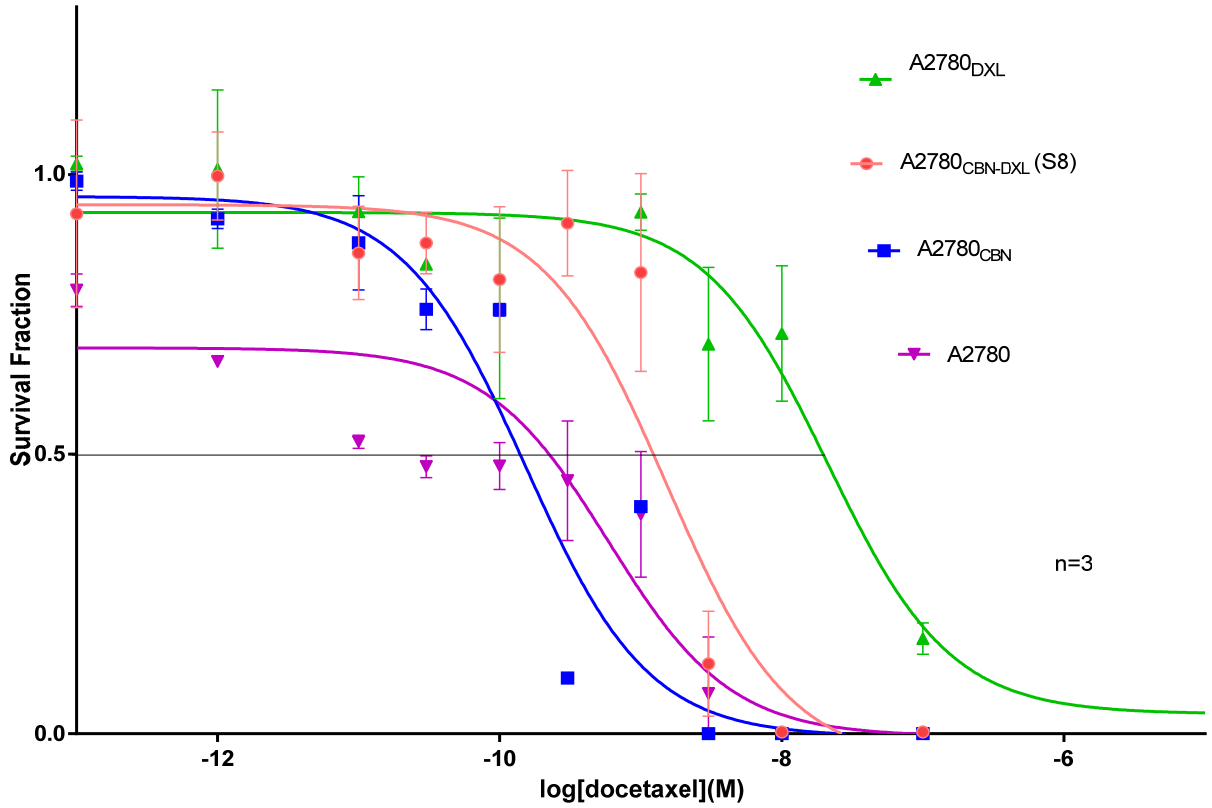


Figure 3.2 Sensitivity of $A2780_{CBN\rightarrow DXL}$, $A2780_{CBN}$, $A2780_{DXL}$, and $A2780_{CC}$ cells to docetaxel, as measured in a clonogenic assay

Dose-response curve showing the relationship of the log of docetaxel concentrations in molarity (M) to the survival fraction of $A2780_{CBN\rightarrow DXL}$ (P25, S8), $A2780_{CBN}$ (P0), $A2780_{DXL}$ (P0), and $A2780_{CC}$ (P0) colonies in varying concentrations of docetaxel. The IC_{50}'s listed are the mean ± SEM of 3 independent experiments.

Table 3.3 Comparisons of IC_{50}'s to docetaxel among cell lines $A2780_{CBN\rightarrow DXL}$, $A2780_{DXL}$, $A2780_{CBN}$, and A2780

Cell lines	$A2780_{CBN\rightarrow DXL}$ (S8,P25) n=3	$A2780_{DXL}$ n=3	$A2780_{CBN}$ n=3	A2780 n=3
IC_{50} (nM)	56	239	0.74	0.49
S.E.M (nM)	9.3	59	0.19	0.22 (1)
p to $A2780_{DXL}$	0.05*			
p to $A2780_{CBN}$	0.008**	0.005*		
p to A2780	0.004**	0.015*	0.44	
Fold change to $A2780_{DXL}$	0.23			
Fold change to $A2780_{CBN}$	76	323		
Fold change to A2780	115	488	1.5	

* Significance of difference ($p<0.05$)

(1) P value was directly calculated from actual clonogenic assay results.

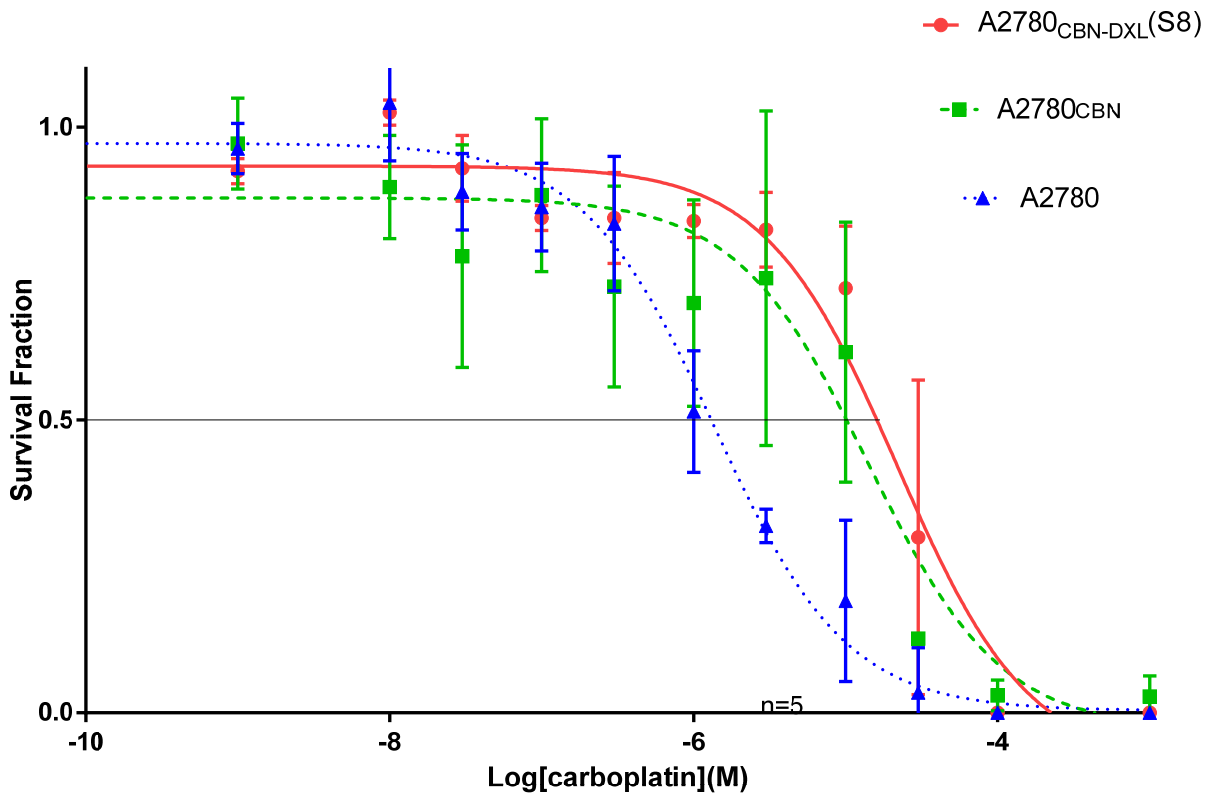


Figure 3.3 $A2780_{CBN \rightarrow DXL}$, $A2780_{CBN}$, $A2780_{CC}$ treated with carboplatin

Dose-response curve showing the relationship of the log of carboplatin concentrations in molarity (M) to the survival fraction of $A2780_{CBN \rightarrow DXL}$ (P25, S8), $A2780_{CBN}$ (P0) and $A2780_{CC}$ (P0) colonies exposed to varying concentrations of carboplatin. The IC_{50}'s listed are the mean ± SEM of 3 independent experiments.

Table 3.4 Comparisons of IC_{50}'s for carboplatin among $A2780_{CBN \rightarrow DXL}$, $A2780_{CBN}$, A2780 cell lines

Cell lines	$A2780_{CBN \rightarrow DXL}$ (S8, P25) n=3	$A2780_{CBN}$ n=3	A2780 n=3
IC_{50} (μM)	18	63	3.8
SEM (μM)	6.8	25	1.8
P to $A2780_{CBN}$	0.19		
p to A2780	0.03*	0.03*	
Fold change to $A2780_{CBN}$	0.29		
Fold change to A2780	4.8	16.5	

* Significance of difference ($p<0.05$)

3.1.3 Characterization of $A2780_{DXL \rightarrow CBN}$ Cells

To determine the effect of selection for carboplatin resistance on prior resistance to docetaxel, a series of clonogenic assays on selected cell lines was performed. To meet this objective, the sensitivity to carboplatin was assessed in the following cells lines: $A2780_{DXL \rightarrow CBN}$, $A2780_{DXL}$, $A2780_{CBN}$, and parental A2780 cells. Carboplatin concentrations ranged from 0.1 nM to 1 mM. The IC_{50} of $A2780_{DXL \rightarrow CBN}$ cells to carboplatin was determined to be 40 ± 2.9 μM, which was significantly higher than that of $A2780_{DXL}$ cells (1.7 ± 0.79 μM carboplatin, resistance factor 24 fold, p=0.0002). However, there was no significant difference (p=0.47) in carboplatin sensitivity between $A2780_{DXL \rightarrow CBN}$ cells (40 ± 2.9 μM carboplatin) and $A2780_{CBN}$ cells (63 ± 2.5 μM carboplatin, resistance factor 0.6 fold) (Figure 3.4, Table 3.5).

Next, the sensitivity of $A2780_{DXL \rightarrow CBN}$ cells to docetaxel was assessed and compared with that of $A2780_{DXL}$ cells and A2780 cells. The cells were treated with docetaxel concentrations ranging from 0.1 pM to 10 μM. The IC_{50} of $A2780_{DXL \rightarrow CBN}$ cells for docetaxel was determined to be 1.8 ± 0.81 nM docetaxel, which was significantly lower than that of the original $A2780_{DXL}$ cell line (238 ± 58 nM docetaxel, resistance factor 135- fold, p=0.016). However, there was no significant difference (p=0.2) in the IC_{50} to docetaxel between $A2780_{DXL \rightarrow CBN}$ cells (1.8 ± 0.081 nM) and parental A2780 cells (0.49 ± 0.22 nM) (Figure 3.5, Table 3.6).

Our results thus showed that $A2780_{DXL}$ cells can acquire carboplatin resistance, and that the original resistance to docetaxel was significantly diminished during selection for carboplatin resistance.

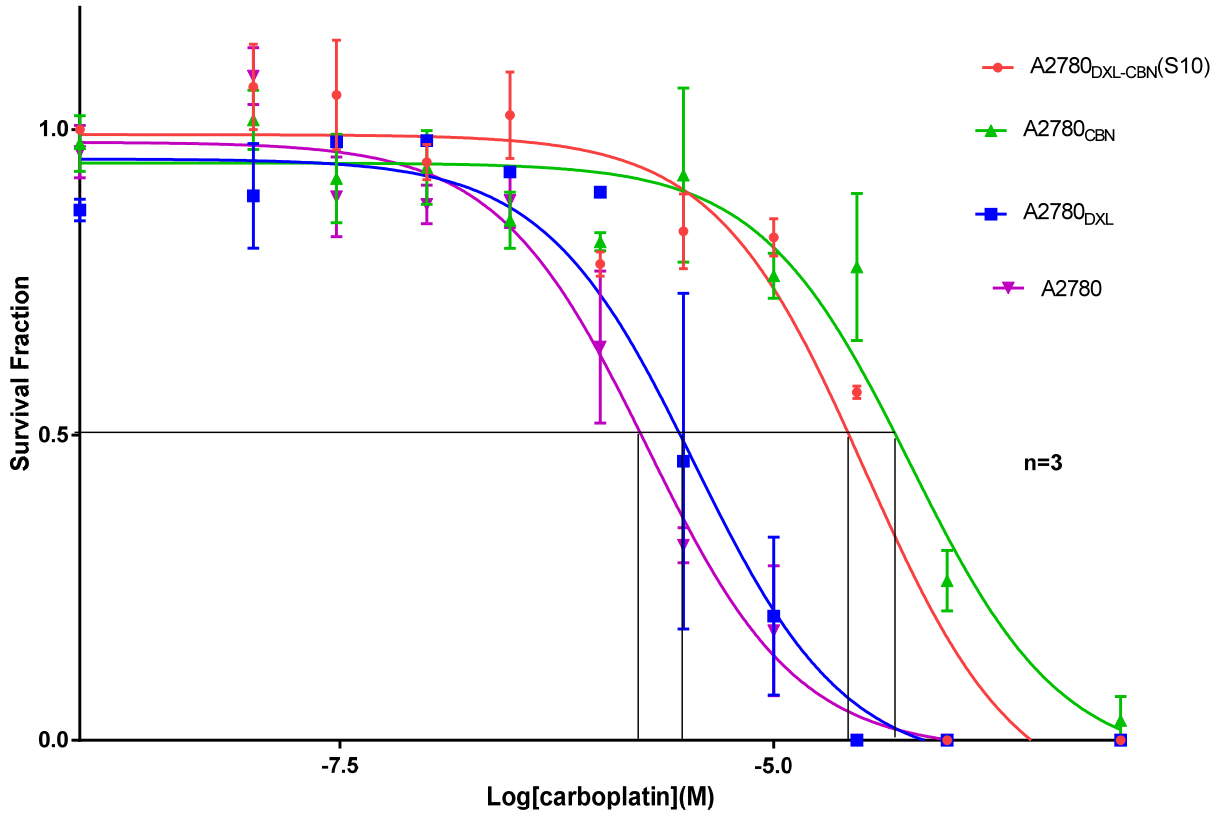


Figure 3.4 $A2780_{DXL\rightarrow CBN}$, $A2780_{DXL}$, $A2780_{CBN}$, $A2780_{CC}$ treated with carboplatin

Dose-response curve showing the relationship between the log of carboplatin concentrations in molarity (M) and the survival fraction of $A2780_{DXL\rightarrow CBN}$ (P29, S10), $A2780_{DXL}$ (P0), $A2780_{CBN}$ (P0) and $A2780_{CC}$ (P0) colonies exposed to varying concentrations of carboplatin. The IC_{50}s listed are the mean ± SEM of 3 independent experiments.

Table 3.5 Comparisons of IC_{50}'s for carboplatin among $A2780_{DXL\rightarrow CBN}$, $A2780_{DXL}$, $A2780_{CBN}$, A2780 cell lines

Cell lines	$A2780_{DXL\rightarrow CBN}$ (S10,P29) n=3	$A2780_{CBN}$ n=3	$A2780_{DXL}$ n=3	A2780 n=3
IC_{50} (μM)	40	63	1.6	3.8
S.E.M (μM)	2.9	2.5	0.79	1.2
p to $A2780_{CBN}$	0.47			
p to $A2780_{DXL}$	0.0002***	0.09		
p to A2780	<0.0001****	0.02*	0.25	
Fold change to $A2780_{CBN}$	0.6			
Fold change to $A2780_{DXL}$	24	38		
Fold change to A2780	10	16		

* Significance of difference ($p<0.05$)

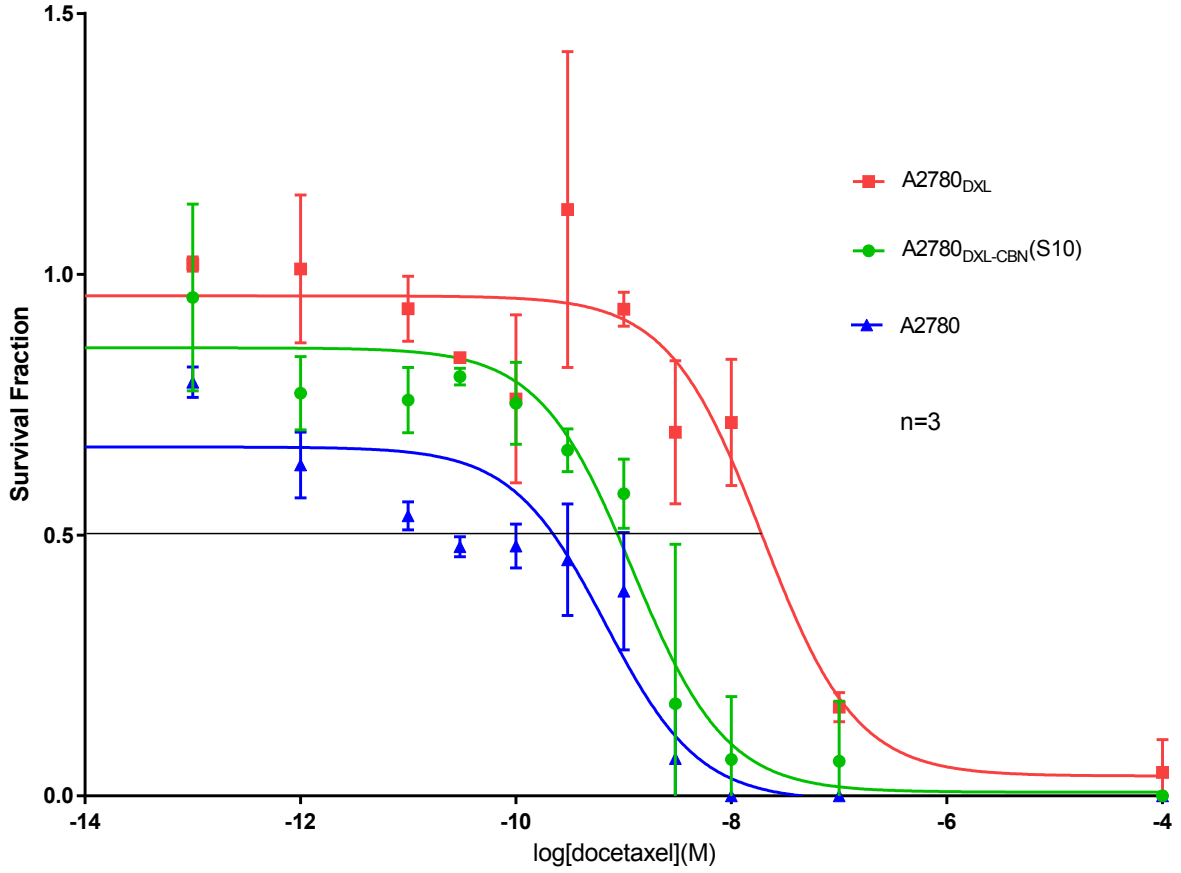


Figure 3.5 $A2780_{DXL \rightarrow CBN}$, $A2780_{DXL}$, $A2780_{CC}$ treated with docetaxel

Dose-response curve comparing log of docetaxel concentrations in molarity (M) to the survival fraction of $A2780_{DXL \rightarrow CBN}$ (P29, S10), $A2780_{DXL}$ (P0) and $A2780_{CC}$ (P0) colonies exposed to varying concentrations of docetaxel. The IC_{50}s listed are the mean ± SEM of 3 independent experiments.

Table 3.6 Comparisons of IC_{50}'s for docetaxel among $A2780_{DXL\rightarrow CBN}$, $A2780_{DXL}$, A2780 cell lines

Cell lines	$A2780_{DXL\rightarrow CBN}$ (S8, P29) n=3	$A2780_{DXL}$ n=3	A2780 n=3
IC_{50} (nM)	1.8	238	0.49
SEM (nM)	0.81	58	0.22
p to $A2780_{DXL}$	0.016*		
p to A2780	0.2	0.015*	
Fold change to $A2780_{DXL}$	0.007		
Fold change to A2780	3.6		

* Significance of difference

3.1.4 Characterization of $A2780_{CBN \rightarrow CC}$ Cells

The $A2780_{CBN \rightarrow CC}$ cell line was established to determine the effect of carboplatin withdrawal on the phenotype of $A2780_{CBN}$ cells. This would also mimic the drug-free interval in terms of withdrawal from carboplatin in ovarian cancer patients in the clinical setting. The $A2780_{CBN \rightarrow CC}$ cells were cultured in drug-free medium until they reached a passage number equal to $A2780_{CBN \rightarrow DXL}$ cells (P25). Sensitivity of $A2780_{CBN \rightarrow CC}$ cells to carboplatin was compared with $A2780_{CBN}$ cells and A2780 cells. The cells were treated with carboplatin ranging from 0.1 nM to 1 mM in concentration. The IC_{50} of $A2780_{CBN \rightarrow CC}$ cells was 18 ± 5.0 μM carboplatin, while for $A2780_{CBN}$ cells it was 63 ± 25 μM carboplatin. This suggested that there was no significant change in the degree of resistance when comparing $A2780_{CBN \rightarrow CC}$ cells to the original $A2780_{CBN}$ parental cells ($p=0.18$) (Figure 3.6, Table 3.7). Therefore, resistance to carboplatin was not significantly altered upon withdrawal of carboplatin in the $A2780_{CBN \rightarrow CC}$ cell line.

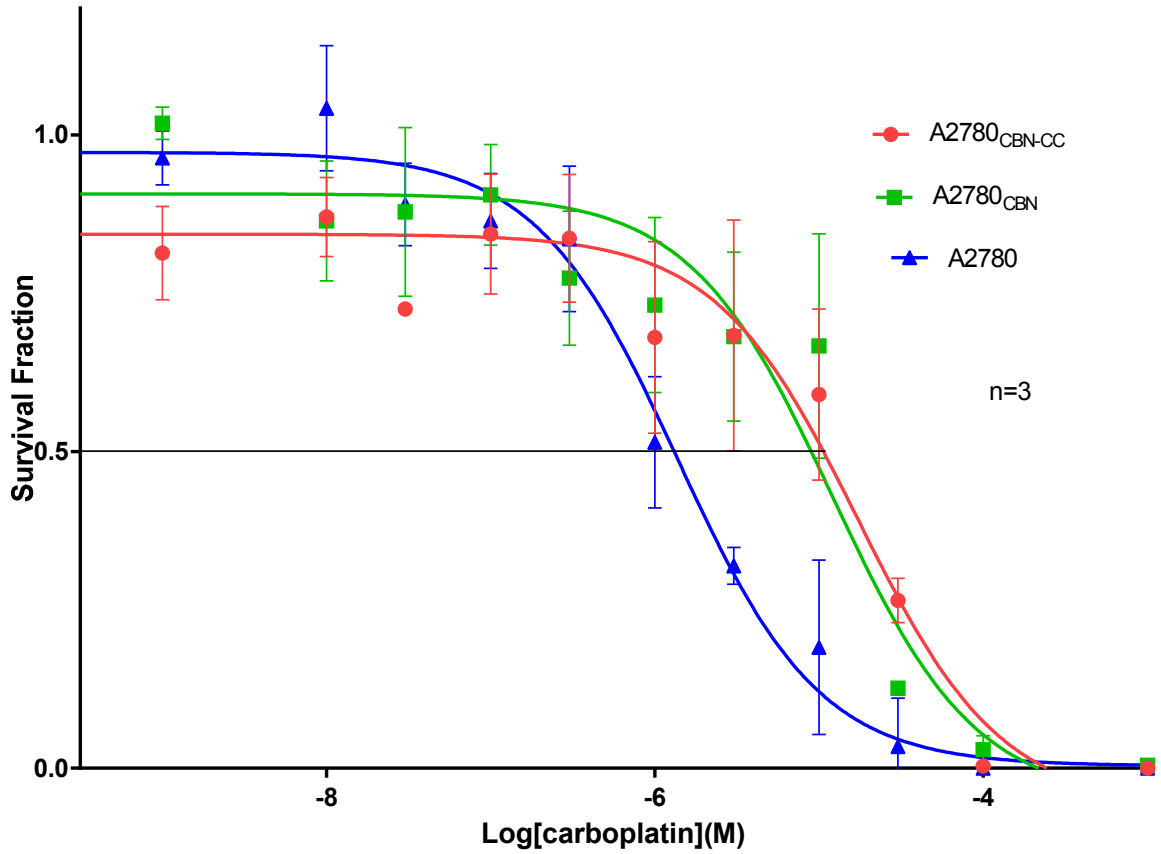


Figure 3.6 A2780$_{CBN\rightarrow CC}$, A2780$_{CBN}$, A2780$_{CC}$ cells treated with carboplatin

Dose-response curve showing the relationship between the log of carboplatin concentrations in molarity (M) to the survival fraction of A2780$_{CBN\rightarrow CC}$ (P0), A2780$_{CBN}$ (P0) and A2780$_{CC}$ (P0) colonies exposed to varying concentrations of carboplatin. The IC$_{50}$'s listed are the mean ± SEM of 3 independent experiments.

Table 3.7 Comparisons of IC_{50}'s for carboplatin among $A2780_{CBN \rightarrow CC}$, $A2780_{CBN}$, and A2780 cell lines

Cell lines	$A2780_{CBN \rightarrow CC}$ (P26) n=3	$A2780_{CBN}$ (P0) n=3	A2780 (P0) n=3
IC_{50} (μM)	18	63	3.8
S.E.M (μM)	5.0	25	1.2
p to $A2780_{CBN}$	0.18		
p to A2780	0.013*	0.03*	
Fold change to $A2780_{CBN}$	0.27		
Fold change to A2780	4.6		

* Significance of difference

3.1.5 Characterization of $A2780_{DXL \rightarrow CC}$ Cells

Likewise, the $A2780_{DXL \rightarrow CC}$ cell line was created to determine the effect of docetaxel withdrawal on the phenotype of $A2780_{DXL}$ cells. This would also represent the clinical situation of docetaxel withdrawal after chemotherapy in ovarian cancer patients. The sensitivity of $A2780_{DXL \rightarrow CC}$ cells to docetaxel was compared to that of parental $A2780_{DXL}$ cells using clonogenic assays. The cells were treated with docetaxel concentrations ranging from 0.1 pM to 10 μM. The IC_{50} of $A2780_{DXL \rightarrow CC}$ cells for docetaxel was determined to be 50 ± 0.30 nM docetaxel. This was a significant reduction in docetaxel resistance when compared to parental $A2780_{DXL}$ cells (239 ± 59 nM docetaxel, $p=0.03$, 5-fold increase in drug sensitivity). Despite the reduction in docetaxel resistance, docetaxel sensitivity was not restored to that of A2780 parental cells (0.50 ± 0.22 nM docetaxel, $p<0.0001$, 102-fold greater sensitivity) (Figure 3.7, Table 3.8). Therefore, the results indicated that resistance to docetaxel was partially but not completely lost through withdrawal of docetaxel.

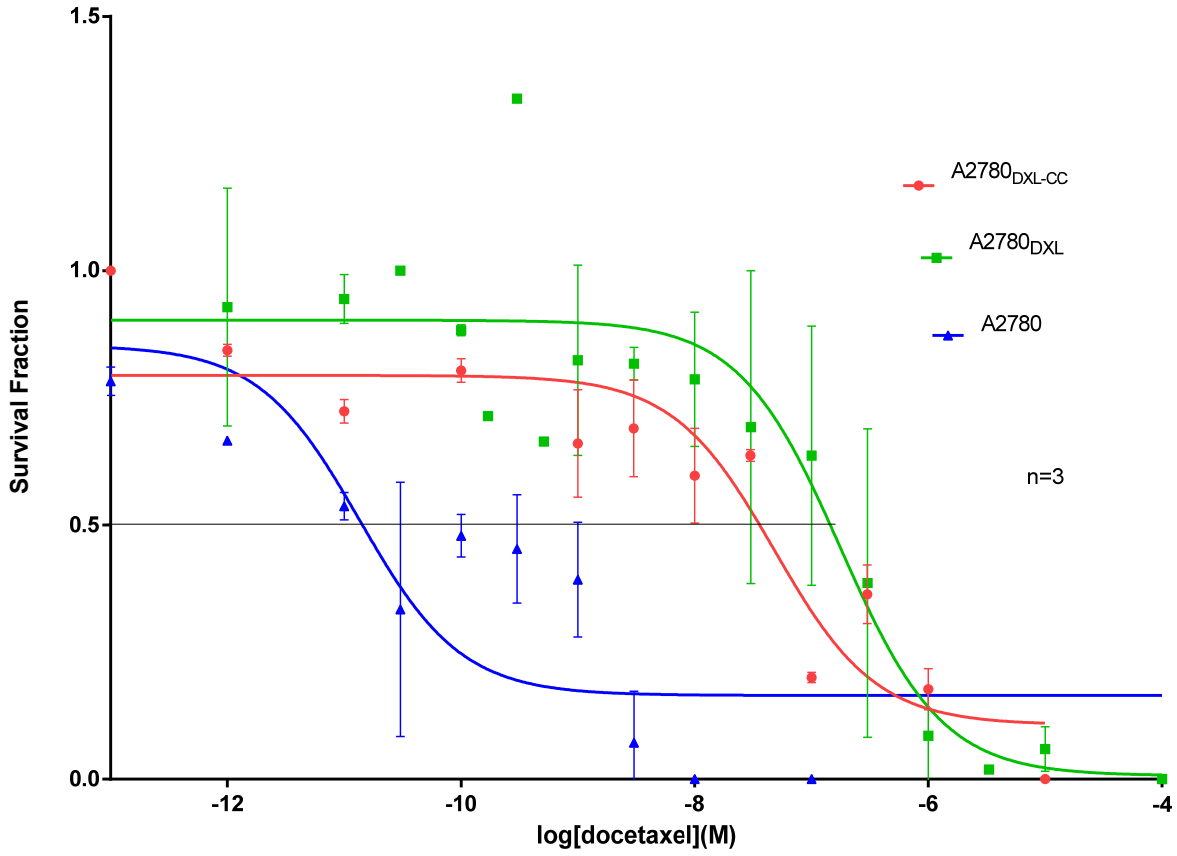


Figure 3.7 $A2780_{DXL \rightarrow CC}$, $A2780_{DXL}$, $A2780_{CC}$ treated with docetaxel

Dose-response curve comparing log of carboplatin concentrations in molarity (M) to the survival fraction of $A2780_{DXL \rightarrow CC}$ (P29), $A2780_{DXL}$ (P0) and $A2780_{CC}$ (P0) colonies exposed to varying concentrations of docetaxel. The IC_{50}s listed are the mean ± SEM of 3 independent experiments.

Table 3.8 Comparisons of IC_{50}'s for docetaxel among $A2780_{DXL\rightarrow CC}$, $A2780_{DXL}$, A2780 cell lines

Cell lines	$A2780_{DXL\rightarrow CC}$ (P29) n=3	$A2780_{DXL}$ (P0) n=3	A2780 (P0) n=3
IC_{50} (nM)	50	239	0.5
S.E.M (nM)	0.3	59	0.22
p to $A2780_{DXL}$	0.03*		
p to A2780	<0.0001****	0.02*	
Fold change to $A2780_{DXL}$	0.21		
Fold change to A2780	102	486	

* Significance of difference

3.2 Gene profile analysis

In this study, microarray experiments involving the hybridization of labeled RNA samples to a very large set of oligonucleotide probes (almost the full human genome) were conducted to detect differences in gene expression between several pairs of the above cell lines. Gene expression differences were then expressed as fold-changes, where positive numbers represented elevated gene expression and negative numbers represented reduced gene expression. Likely, both drug withdrawal and selection for resistance to a new anti-cancer drug precipitated the observed positive and negative changes in gene expression.

3.2.1 Comparison of Gene Expression between $A2780_{CBN \rightarrow DXL}$ and $A2780_{CBN}$ Cells

$A2780_{CBN \rightarrow DXL}$ (P25, S8) and $A2780_{CBN}$ (P1) cells were cultured in drug-free medium for 48 hours, after which total RNA was extracted from both cell lines. All RNA preparations with RIN values between 9.0 and 10.0 were deemed suitable for microarray analysis. Upon completion of the microarray experiments, we noted all genes whose expression wassignificantly different ($p \leq 0.05$) by ≥2-fold between the Cy-3 labelled and Cy-5 labelled cRNA preparations, with a false discovery rate (FDR) set at 0.01. A total of 1115 significant differences in gene expression were detected between the $A2780_{CBN \rightarrow DXL}$ and $A2780_{CBN}$ cell lines. Of these genes, 586 were up-regulated in the $A2780_{CBN \rightarrow DXL}$ cell line compared to the $A2780_{CBN}$ cell line, while 547 were down-regulated (Table 3.9). All differences in expression between the $A2780_{CBN \rightarrow DXL}$ and $A2780_{CBN}$ cell lines are described in Appendix I.

3.2.2 Comparison of Gene Expression between $A2780_{CBN \rightarrow CC}$ and $A2780_{CBN}$ Cells

$A2780_{CBN\rightarrow CC}$ (P24) and $A2780_{CC}$ (P24) cells were cultured in drug-free medium for 48 hours, after which total RNA was extracted from both cell lines. All RNA preparations with RIN values between 9.0 and 10.0 were deemed suitable for microarray analysis. Using the same criteria as described for microarray-based comparisons between $A2780_{CBN\rightarrow DXL}$ and $A2780_{CBN}$ cells, a total of 3189 genes were identified whose expression was differentially expressed between $A2780_{CBN\rightarrow CC}$ and A2780 cells. Of these, 741 genes were up-regulated in the $A2780_{CBN\rightarrow CC}$ cell line compared to the A2780 cell line, while 2289 were down-regulated (Table 3.9). All differences in gene expression between the $A2780_{CBN\rightarrow CC}$ and A2780 cell lines are described in Appendix II.

3.2.3 Comparison of Gene Expression between $A2780_{CBN\rightarrow DXL}$ and $A2780_{DXL}$ Cells

Gene expression differences between $A2780_{CBN\rightarrow DXL}$ and $A2780_{DXL}$ cells were identified using a "between array" comparison method (see section 2.4.6). Using the same criteria that were used in the above analyses, 3910 genes were up-regulated in the $A2780_{CBN\rightarrow DXL}$ cell line compared to the $A2780_{DXL}$ cell line, and 1805 were down-regulated, for a total of 5715 changes in gene expression (Table 3.9). All differences in gene expression between the $A2780_{CBN\rightarrow DXL}$ and $A2780_{DXL}$ cell lines are described in Appendix III.

3.2.4 Comparison of Gene Expression between $A2780_{CBN\rightarrow CC}$ and $A2780_{CC}$ Cells

A similar "between array" comparison of gene expression was conducted using the microarray datasets comparing gene expression between the $A2780_{CBN\rightarrow CC}$ and $A2780_{CC}$ cell lines and between the $A2780_{CBN\rightarrow DXL}$ and $A2780_{CBN}$ cell lines. This enabled us to identify 695 genes that were up-regulated in the $A2780_{CBN\rightarrow CC}$ cell line compared to the $A2780_{CC}$ cell line, and 490 that

were down-regulated, for a total of 1185 changes in gene expression (Table 3.9). All changes in expression in the $A2780_{CBN \rightarrow CC}$ and $A2780_{CC}$ line are described in Appendix IV.

Table 3.9 Number of up-regulated, down-regulated and total gene expression changes in the four $A2780_{CBN}$-variants comparison (FDR=0.01, $p \leq 0.05$)

Comparison	Up-regulated	Down-regulated	Total
$A2780_{CBN \rightarrow DXL}$ vs $A2780_{CBN}$	586	547	1115
$A2780_{CBN \rightarrow CC}$ vs $A2780_{CBN}$	741	2448	3189
$A2780_{CBN \rightarrow DXL}$ vs $A2780_{DXL}$	3910	1805	5715
$A2780_{CBN \rightarrow CC}$ vs $A2780_{CC}$	695	490	1185

3.2.5 Comparison of Gene Expression between $A2780_{DXL\rightarrow CBN}$ and $A2780_{DXL}$ Cells

Using RNA isolated from $A2780_{DXL\rightarrow CBN}$ and $A2780_{DXL}$ cells, identical microarray studies were conducted (using the same collection criteria) to identify 1418 genes up-regulated in $A2780_{DXL\rightarrow CBN}$ cells compared to $A2780_{DXL}$ cells, and 1081 down-regulated genes (Table 3.10). All differences in gene expression between the $A2780_{DXL\rightarrow CBN}$ and $A2780_{DXL}$ cell lines are described in Appendix V.

3.2.6 Comparison of Gene Expression between $A2780_{DXL\rightarrow CC}$ and $A2780_{DXL}$ Cells

An identical approach also identified 5051 differences in gene expression between $A2780_{DXL\rightarrow CC}$ and A2780cc cells. Of these, 1420 genes were up-regulated and 3631 were down-regulated (Table 3.10). All differences in gene expression between $A2780_{DXL\rightarrow CC}$ and A2780 cells are described in Appendix VI.

3.2.7 Comparison of Gene Expression between $A2780_{DXL\rightarrow CBN}$ and $A2780_{CBN}$ Cells

In yet another identical approach, 1503 genes were found to be up-regulated in $A2780_{DXL\rightarrow CBN}$ cells compared to A2780CBN cells, while 3268 were down-regulated, for a total of 4771 changes in gene expression (Table 3.10). All differences in gene expression between the $A2780_{DXL\rightarrow CBN}$ and $A2780_{CBN}$ cell lines are described in Appendix VII.

3.2.8 Comparison of Gene Expression between $A2780_{DXL\rightarrow CC}$ and $A2780_{CC}$ Cells

Finally, 783 genes were up-regulated (and 940 downregulated) in the $A2780_{DXL\rightarrow CC}$ cell line compared to the $A2780_{CC}$ cell line, for a total of 1723 differences in gene expression (Table

3.10). All differences in gene expression between the $A2780_{DXL\rightarrow CC}$ and $A2780_{DXL}$ cell lines are described in Appendix VIII.

Table 3.10 Number of up-regulated, down-regulated and total gene expression changes in the four $A2780_{DXL}$-variant comparison pairs (FDR=0.01, $p \leq 0.05$)

Comparison	Up-regulated	Down-regulated	Total
$A2780_{DXL\rightarrow CBN}$ vs $A2780_{DXL}$	1418	1081	2499
$A2780_{DXL\rightarrow CC}$ vs $A2780_{DXL}$	1420	3631	5051
$A2780_{DXL\rightarrow CBN}$ vs $A2780_{CBN}$	1503	3268	4771
$A2780_{DXL\rightarrow CC}$ vs $A2780_{CC}$	783	940	1723

3.3 Analyses of Gene Expression Profiles for Acquired and Previous Drug Resistance

3.3.1 Gene Expression Changes Related to Acquisition of Docetaxel Resistance in $A2780_{CBN \rightarrow DXL}$ Cells

Our clonogenic studies of $A2780_{CBN \rightarrow DXL}$ cells suggested that docetaxel resistance is established when $A2780_{CBN}$ cells are selected for survival in increasing concentrations of docetaxel. The focus was then on how docetaxel resistance is established and whether previous carboplatin resistance is maintained and/or influenced by the new phenotype. In our microarray data analyses, the comparison between $A2780_{CBN \rightarrow DXL}$ vs. $A2780_{CBN}$ cells included gene expression changes that are likely associated with the acquisition of docetaxel resistance due to exposure to increasing concentrations of docetaxel in the absence of carboplatin. On the other hand, in the comparison between $A2780_{CBN \rightarrow CC}$ vs. A2780 cells, the gene expression changes would likely reflect the effects of long-term cell culture in the absence of carboplatin selective pressure. Therefore, by comparing the two sets of altered genes, we can likely differentiate genes key to the establishment of docetaxel resistance from genes associated with the loss of carboplatin selective pressure, which may reflect the effects of long-term cell culture in the absence of carboplatin selective pressure (Figure 3.8 C). The resulting list of 435 genes is featured in Appendix IX. Of the genes associated with the acquisition of docetaxel resistance, we placed particular emphasis on those changing expression by 10-fold or greater (Table 3.11).). Interestingly, 8 of the 14 genes listed in Table 3.11 also differentially expressed in the original $A2780_{DXL}$ line, when compared to the parental A2780 line, indicating an association with docetaxel resistance. Some of the genes, for example CFH, RND3, PRR7, PRL showed changes in opposite direction from the original $A2780_{DXL}$ line while BEX1, HAPLN1, SULF2, and ATP6V0D2 changed in the same direction (upregulation) although usually to a greater extent in

the reverse selected $A2780_{CBN \rightarrow DXL}$ cell line.(unpublished data provided by Dr. Carita Lannér. See Table 3.11 column "fold change $A2780_{DXL}$ vs. A2780")

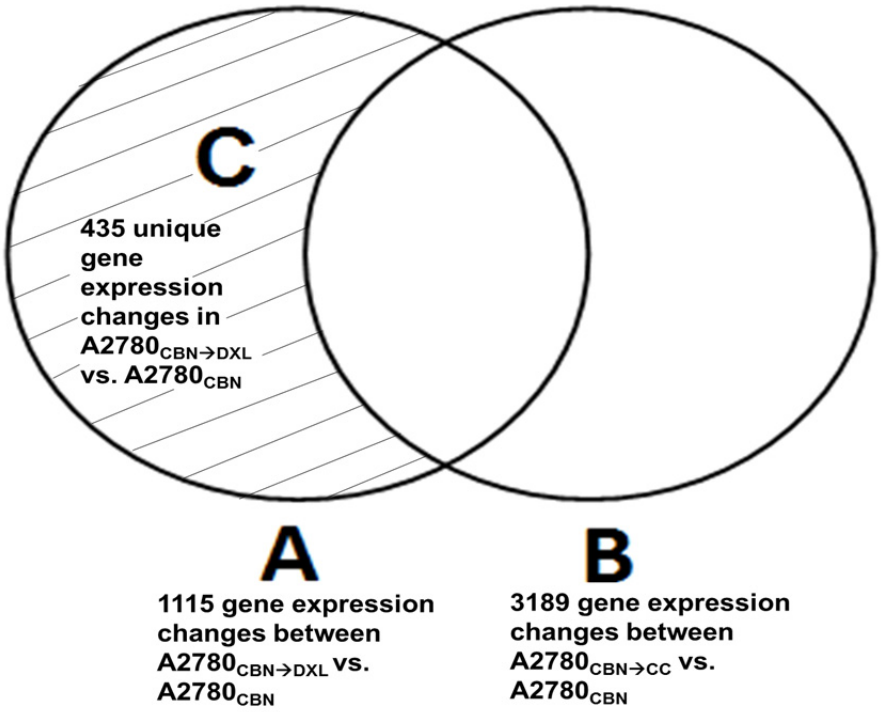


Figure 3.8 Gene Expression differences between the $A2780_{CBN}$ cell line and the $A2780_{CBN\rightarrow DXL}$, $A2780_{CBN}$, and $A2780_{CBN\rightarrow CC}$ cell lines

(A) Gene expression changes in $A2780_{CBN\rightarrow DXL}$ vs. $A2780_{CBN}$; (B) Gene expression changes in $A2780_{CBN\rightarrow CC}$ vs. $A2780_{CBN}$. (C) After merging two sets of comparisons, 435 unique gene changes appear to be associated with the establishment of docetaxel resistance in the $A2780_{CBN\rightarrow DXL}$ cell line.

Table.3.11 Gene expression changes (>10-fold) upon establishment of docetaxel resistance in the $A2780_{CBN \rightarrow DXL}$ cell line.

These genes are unrelated to those changing expression upon loss of carboplatin selective pressure.

Gene name	Protein name	Fold change $A2780_{CBN \rightarrow DXL}$ vs $A2780_{CBN}$	p for fold change	fold change $A2780_{DXL}$ vs. A2780 [(1)]
CFH	Complement Factor H	-13.99	10.9 x 10-4	2.19
AKR1C1	aldo-keto reductase family 1, member C1	-11.76	1.54 x 10-4	-6.35
CFHR3	complement factor H-related	-11.61	2.76 x 10-4	6.48
A2M	Alpha-2-Macroglobulin	-10.39	8.22 x 10-4	
RND3	Rho family GTPase 3	15.31	4.22 x10-4	-2.00
BEX1	brain-expressed X-linked protein 1	15.50	4.10 x 10-4	-10.00
PRR16	proline rich 16	15.99	7.22 x 10-4	6.23
PRL	Prolactin	16.63	6.89 x 10-4	
HAPLN1	hyaluronan and proteoglycan link protein 1	17.13	1.04 x 10-4	2.66
SULF1	Sulfatase 1	18.36	2.84 x 10-4	2.29
MECOM	MDS1 and EVI1 complex locus	20.32	5.00 x 10-4	
SLITRK6	SLIT and NTRK-like family, member 6	21.75	5.40 x 10-4	
ATP6V0D2	ATPase, H+ transporting, lysosomal 38kDa, V0 subunit d2	35.69	6.93 x 10-4	

(1) Unpublished data provided by Dr. Carita Lannér.

3.3.2 Microarray Analyses Support No Significant Expression Changes for Genes Associated with Carboplatin Sensitivity in the $A2780_{CBN \rightarrow DXL}$ and $A2780_{CBN \rightarrow CC}$ Cells

The previous clonogenic assay results showed that carboplatin sensitivity (the IC_{50}) for $A2780_{CBN \rightarrow DXL}$ cells was similar to that of $A2780_{CBN \rightarrow CC}$ cells, when each cell type was compared to $A2780_{CBN}$ cells (i.e. not significantly different from a statistical point of view*). These two cell lines were not compared directly to one another.* This suggests that the carboplatin resistance phenotype in $A2780_{CBN}$ cells was not lost upon withdrawal of carboplatin selective pressure, even if this involved exposure to a new chemotherapy agent (docetaxel). Previous microarray studies published by Armstrong *et al*. [150]suggested that down-regulation of *ANXA1* and up-regulation of *CDH7*, *GLCL*, *GSTO1* and *PARP9* were related to acquired carboplatin resistance by comparing gene expression between $A2780_{CBN}$ and A2780 cells (Table 3.12). To know if the expression of these 5 genes was altered by carboplatin withdrawal in the current study, I searched the gene names in the microarray data files comparing gene expression between $A2780_{CBN \rightarrow DXL}$ and $A2780_{CBN}$ cells and between $A2780_{CBN\text{-}CC}$ and $A2780_{CBN}$ cells. This analysis showed that the expression of the above 5 genes was not significantly changed upon withdrawal from carboplatin selective pressure, except for *GCLC* (which encodes the glutamate-cysteine ligase catalytic subunit). The expression of this gene was down-regulated approximately 2-fold upon withdrawal of carboplatin selective pressure. In contrast, *GCLC* was up-regulated 8.5 times in Armstrong et al.'s comparison of gene expression between $A2780_{CBN}$ and A2780 cells. Therefore, expression of these genes were not altered upon selection of $A2780_{CBN}$ cells for resistance to docetaxel ($A2780_{CBN \rightarrow DXL}$ cells) or upon withdrawal of carboplatin selective pressure in $A2780_{CBN}$ cells ($A2780_{CBN \rightarrow CC}$ cells).

Table 3.12 The comparison of gene expression related to carboplatin resistance in microarray analysis profiles

Gene Name	Protein Name	General function	Fold change $A2780_{CBN}$ vs $A2780^{(1)}$	$P^{(1)}$	Fold change $A2780_{CBN \rightarrow DXL}$ vs $A2780_{CBN}$	P	Fold change $A2780_{CBN \rightarrow CC}$ vs $A2780_{CBN}$	P
ANXA1	Annexin A1	Calcium dependent phospholipid binding protein	-104.15	$1.38x10^{-4}$	N/A [2]	N/A	N/A	N/A
CDH7	Cadherin 7	Cell to cell adhesion glycoprotein	2.08	$1.29x10^{-4}$	N/A	N/A	N/A	N/A
GCLC	Glutamate-cysteine ligase catalytic subunit	Rate limiting enzyme of glutathione synthesis	8.50	$5.85x10^{-5}$	-2.18	$8.65x10^{-5}$	-2.44	1.62×10^{-5}
GSTO1	Glutathion S-transferase omega 1	Stress response protein, catalyzes addition of glutathione to toxic substrates	2.38	$1.07x10^{-3}$	N/A	N/A	N/A	N/A
PARP9	Poly(ADP)-ribose polymerase family member 9	Catalyzes addition of ADP-ribose moieties to substrate proteins	9.40	$1.95x10^{-3}$	N/A	N/A	N/A	N/A

(1) Data retrieved from previous work: S. Armstrong, R. Narendrula, Baoqing Guo, A. Parissenti, K. McCallum, S. Cull, C. Lannér. Distinct genetic alterations occur in ovarian tumour cells selected for combined resistance to carboplatin and docetaxel. Journal of Ovarian Research. 2012, 5:4

(2) No fold changes were identified in the paired cell lines.

3.3.3 Gene Expression Changes Related to Acquisition of Carboplatin Resistance in $A2780_{DXL\rightarrow CBN}$ Cells

According to clonogenic assay data, carboplatin resistance was achieved in the established $A2780_{DXL\rightarrow CBN}$ cell line by exposing $A2780_{DXL}$ cells to carboplatin in the absence of docetaxel. On the other hand, the gene expression changes identified from microarray experiments involving $A2780_{DXL\rightarrow CBN}$ and $A2780_{DXL}$ cells would be expected to include genes involved in both the establishment of carboplatin resistance (Armstrong *et al*.) and the loss of docetaxel resistance after long term culture. Meanwhile, since docetaxel resistance was also lost upon removal of docetaxel selective pressure in $A2780_{DXL\rightarrow CC}$ cells (confirmed by clonogenic assays), the gene expression changes identified in microarray experiments comparing $A2780_{DXL\rightarrow CC}$ cells with $A2780_{DXL}$ cells would be expected to be associated with the loss of docetaxel resistance. Therefore, we merged the data from two comparison pairs, ($A2780_{DXL\rightarrow CBN}$ cells vs. $A2780_{DXL}$ cells and $A2780_{DXL\rightarrow CC}$ cells vs. $A2780_{DXL}$ cells), to exclude genes associated with docetaxel resistance loss (Figure 3.9 D) in order to reveal the genes specifically associated with acquisition of carboplatin resistance (Figure 3.9 C). Through this approach, 1319 unique changes in gene expression were identified to be associated with the acquisition of carboplatin resistance [$A2780_{DXL\rightarrow CBN}$ cells vs. $A2780_{DXL}$ cells (Figure 3.9 C)]. These genes are listed in Appendix X.

Among these genes, we noted those changing expression by 10-fold or greater (Table 3.14). Several of these genes are involved in apoptotic pathways (*BEX1* [161], Brain-expressed X-linked protein 1; *BCL6* [162–164], B-cell CLL/lymphoma 6; *CYB5A* [165,166], cytochrome b5 type A; *CYB5R2*, cytochrome b5 reductase 2; *SLC25A24* [167–169], solute carrier family 25 member 24; and *FAS* [170,171], cell surface death receptor).

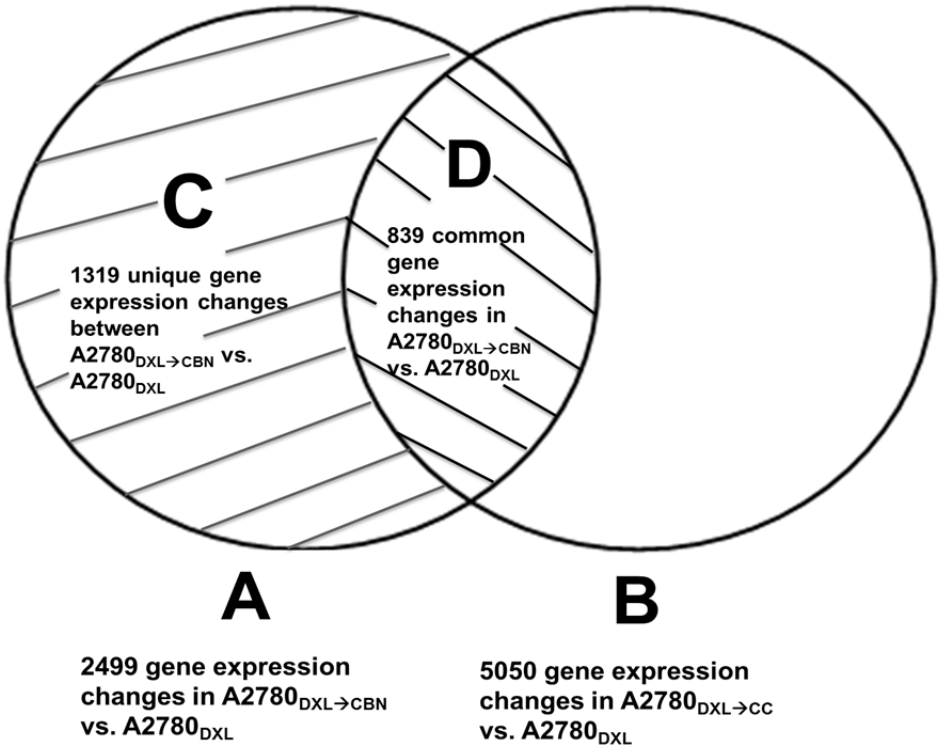


Figure 3.9 Gene expression differences between $A2780_{DXL\rightarrow CBN}$ and $A2780_{DXL}$ cells and between $A2780_{DXL\rightarrow CC}$ and $A2780_{DXL}$ cells

(A) Gene expression differences between $A2780_{DXL\rightarrow CBN}$ and $A2780_{DXL}$ cells; (B) gene expression differences between $A2780_{DXL\rightarrow CC}$ and $A2780_{DXL}$ cells; (C) common gene expression differences between (A) and (B) that may be associated with the loss of docetaxel resistance; (D) unique gene expression changes that may be associated with carboplatin resistance establishment in the $A2780_{DXL\rightarrow CBN}$ cell line.

Table 3.13 Gene expression differences that may be related to the establishment of carboplatin resistance in the $A2780_{DXL \rightarrow CBN}$ cell line

Gene name	Protein name	General function	Fold change $A2780_{DXL \rightarrow CBN}$ vs. $A2780_{DXL}$	p for fold change
BEX1	Brain-expressed X-linked protein 1	Inhibition of apoptosis by down-regulation of hBEX1	-137.99	3.92×10^{-5}
BCL6	B-cell CLL/lymphoma 6	Apoptosis inhibitor	15.52	3.82×10^{-4}
CYB5A	cytochrome b5 type A	Autophagy induction	-25.48	1.23×10^{-4}
CYB5R2	cytochrome b5 reductase 2	drug metabolism	-10.15	1.09×10^{-5}
SLC25A24	solute carrier family 25, member 24	Calcium-dependent mitochondrial solute carrier	793.5	7.6×10^{-5}
FAS	Fas cell surface death receptor	death receptor on the surface of cells leading apoptosis	-10.87	1.23×10^{-5}
PITX2	paired-like homeodomain transcription factor 2	ABCB1 binding factor	220.32	1.31×10^{-4}
EMP1	Epithelial membrane protein-1	Gefitinib resistance biomarker	506.23	7.01×10^{-5}

3.3.4 Possible Gene Expression Changes Associated with Diminished Docetaxel Resistance in $A2780_{DXL\rightarrow CBN}$ and $A2780_{DXL\rightarrow CC}$ Cells

According to clonogenic assay results involving the $A2780_{DXL\rightarrow CBN}$ and $A2780_{DXL\rightarrow CC}$ cell lines, docetaxel resistance was still observed (but at a substantially lower level) after removal of docetaxel selective pressure. The focus then became on how docetaxel resistance became reduced in those cells. Previous microarray data [150] (Armstrong *et al.*) suggested that up-regulation of *ABCB1* (33.6-fold) and *ABCB4* (141-fold) expression, and down-regulation of *CYP1B1* expression (-38 fold) were associated with acquisition of docetaxel resistance [comparison of $A2780_{DXL}$ and A2780 cells (table 3.14)]. To determine whether these genes were also altered by docetaxel withdrawal, we examined the expression data for the above genes in the microarray comparisons between $A2780_{DXL\rightarrow CBN}$ cells and $A2780_{DXL}$ cells and between $A2780_{DXL\rightarrow CC}$ cells and $A2780_{DXL}$ cells. This analysis showed that the above three genes did, again, exhibit changes in gene expression, but in the opposite direction. *ABCB1* expression was down-regulated 15-28 times, while *ABCB4* was downregulated 9-131 times. *CYP1B1* expression was upregulated 6-68 times (Table 3.14). This comparison suggests that these genes are truly associated with docetaxel resistance, as they changed in the positive direction upon acquisition of docetaxel resistance and, in tandem, in the negative direction when docetaxel selective pressure was removed and docetaxel resistance was lost.

Table 3.14 Genes related to reduced docetaxel resistance in microarray studies

Gene name	Protein name	General function	Fold change $A2780_{DXL}$ vs A2780cc[(2)]	P [(2)]	Fold change $A2780_{DXL\searrow CBN}$ vs $A2780_{DXL}$	P	Fold change $A2780_{DXL\searrow CC}$ vs $A2780_{DXL}$	P
CYP1B1	Cytochrome P450 family 1, subfamily B, polypeptide 1	Phase 1 enzyme in drug metabolism	–37.77	2.0×10^{-8}	67.54	7.2×10^{-5}	5.96	4.34×10^{-6}
ABCB1	ATP-binding cassette transport subfamily B, member 1	Multidrug transporter (MDR/TAP family)	33.62	8.2×10^{-11}	-27.8	1.6×10^{-6}	-14.73	6.59×10^{-8}
ABCB4	ATP-binding cassette transport subfamily B, member 4	Multidrug transporter (MDR/TAP family)	141.27	5.8×10^{-10}	-130.99	1.2×10^{-4}	-9.25	2.7×10^{-7}

(2) Data retrieved from previous work (S. Armstrong, R. Narendrula, Baoqing Guo, A. Parissenti, K. McCallum, S. Cull, C. Lannér. Distinct genetic alterations occur in ovarian tumour cells selected for combined resistance to carboplatin and docetaxel. Journal of Ovarian Research. 2012, 5:4

Chapter 4

4. Discussion

Ovarian cancer remains the leading cause of death for gynecologic malignancies in North America [1,2]. Chemotherapy still plays a major role in treatment and is employed after surgery (adjuvant chemotherapy), although neoadjuvant chemotherapy has been used to treat some ovarian cancer patients with reasonable efficacy [3,4]. Since the 1990s, the combination of taxane and platinating agents became the preferred (standard) regimen for chemotherapy treatment of ovarian cancer patients [2,18–20,172]. The initial response rate for this regimen can be as high as 70%, but eventually these patients will relapse and possess chemo-resistant tumours [18]. Thus, the 5-year survival rate post-treatment remains low statistically. Innate or acquired drug resistance in tumours is one of the major obstacles to the effective treatment of advanced ovarian cancer. To understand the mechanisms contributing to drug resistance in ovarian tumour cells, our lab has focused its efforts on characterizing newly established ovarian tumour cell lines that have been selected for resistance to a platinating agent (after resistance to a taxane has been achieved) and selected for resistance to a taxane (after resistance to a platinating agent has been achieved). We hypothesized that exposure to platinating agents may rapidly re-establish tumour cell sensitivity to taxanes and *vice versa,* possibly at a faster rate than by simple drug withdrawal.

In the end of the experiments, each cell line underwent microarray analysis to identify changes in gene expression that accompany loss of selection pressure and/or acquisition of resistance to a new chemotherapy agent.

The drugs used in our study included both carboplatin and docetaxel, since the original resistant A2780 cell lines had been derived using these agents and because there was no cross resistance between these drugs [150]. Carboplatin was chosen as the platinating agent because it is clinically preferred, with less toxicity and longer lasting effects when compared to cisplatin [56]. Docetaxel was chosen for the study because docetaxel also has a more favorable toxicity profile, since its major toxic side effect (neutropenia) can be managed with other agents such as pegfilgrastim [173,174], and since docetaxel does not induce the same degree of neuropathy as paclitaxel [82,175].

During the selection process for carboplatin or docetaxel resistance, the drug concentration was gradually elevated from the first selection dose (S1) to the maximally tolerated dose. Dead cells were observed in the culture flask during selection, suggesting that some of the cells were unable to survive while other cells possessed or developed resistance to the drugs at the specific selection doses. It is notable that at the end of the selection for the $A2780_{DXL \rightarrow CBN}$ subline, these cells exhibited a clear morphology change compared to the $A2780_{DXL}$ cell line from which it was derived (Fig 3.1). $A2780_{DXL \rightarrow CBN}$ cells were more spindle-shaped compared to the oval-shaped $A2780_{DXL}$ cells. Meanwhile, a morphology change was not observed when $A2780_{CBN}$ cells were selected for resistance to docetaxel ($A2780_{CBN \rightarrow DXL}$ cells). This suggests that the morphology change is associated with acquisition of carboplatin resistance after prior selection for docetaxel resistance (and not *vice versa*). In many studies, this kind of morphology change of $A2780_{DXL \rightarrow CBN}$ cells takes place during the epithelial mesenchymal transition (EMT) [176,177]. Cells undergoing EMT usually exhibit loss of epithelial polarity, increased motility and migration characteristics [178,179], suggesting that they have progressed to a more invasive state. Therefore, the changes in morphology (round to spindle for the transition from $A2780_{DXL}$ cells to $A2780_{DXL \rightarrow CBN}$ cells) are considered to be associated with increased tumour aggressiveness.

Moreover, studies also have shown that EMT can be related to drug resistance in different cancers. According to Sayan *et al*., the expression of EMT-associated genes *ZED2* and *SIP1* in muscle-invasive urothelial cancer cells protects the cells from DNA damage-induced apoptosis [180].

In our microarray studies, when comparing gene expression changes between $A2780_{DXL \rightarrow CBN}$ and $A2780_{DXL}$ cells (see Appendix V), several genes related to EMT are identified through cross-referencing with Qiagen's list of genes associated with the EMT in their EMT PCR array (http://www.sabiosciences.com/rt_pcr_product/HTML/PAHS-090Z.html) [181-182].

Table 4.1 EMT related genes that exhibit expression change as $A2780_{DXL}$ cells are selected for resistance to carboplatin ($A2780_{DXL \rightarrow CBN}$ cells)

Gene name	Protein name	General function	Fold change $A2780_{DXL \rightarrow CBN}$ vs. $A2780_{DXL}$	p for fold change
ITGAV	Integrin subunit alpha V	vitronectin receptor	4.65	1.29×10^{-5}
MMP3	Matrix metallopeptidease 3	Degrade fibronectin, laminin, collagens,	73.47	4.75×10^{-4}
S100A4	S100 calcium binding protein A4	motility, invasion, and tubulin polymerization	2.22	1.19×10^{-3}
SDC2	syndecan 2	cell binding, signaling, and cytoskeletal organization	32.03	1.18×10^{-4}
SPARCL1	SPARC like 1	Cell migration	8.46	5.27×10^{-4}
TCF4	transcription factor 4	immunoglobulin enhance	4.15	2.32×10^{-5}
VPS13A	vacuolar protein sorting 13 homolog A	cycling of proteins through the trans-Golgi network	2.15	1.05×10^{-3}
COL2A1	collagen type II alpha 1	fibrillar collagen	-5.66	2.81×10^{-4}
SPP1	secreted phosphoprotein 1	bone mineralization	-69.08	7.11×10^{-6}

Clonogenic assays were performed for quantification of cellularity sensitivity to the above chemotherapy drugs. This assay is considered to be more sensitive and more accurate than high throughput colorimetric , such as the 3-(4, 5-dimethylthiazol-2-yl) 2, 5-diphenyl-tetrazolium bromide (MTT) assay. The MTT assay indirectly measures cell viability by quantifying the ability of a mitochondrial dehydrogenase enzyme in cells to convert the tetrazolium salt into formazan [183]. However, the enzyme exists not only in metabolically active cells but also in dead cells [184,185]. This results in the MTT assay overestimating cell viability. It is therefore not as accurate as the clonogenic assay (despite its ease of use).

In previous studies, resistance to docetaxel ($A2780_{DXL}$ cells) and carboplatin ($A2780_{CBN}$ cells) were established by treating A2780 cells with increasing doses of docetaxel or carboplatin, with retention of surviving cells [186]. The resistant cell lines were very stable in liquid nitrogen storage. The clonogenic assay results (Fig 3.2) indicated that the $A2780_{CBN\rightarrow DXL}$ cell line exhibits considerably greater resistance to docetaxel than parental $A2780_{CBN}$ cells. The IC_{50} for docetaxel of $A2780_{CBN\rightarrow DXL}$ cells was 76 times higher than that of $A2780_{CBN}$ cells and 4 times lower than that of $A2780_{DXL}$ cells. However, there was no statistically significant difference in docetaxel sensitivity (IC_{50}) between $A2780_{CBN\rightarrow DXL}$ and $A2780_{DXL}$ cells (p=0.05, table 3.3), indicating that the degree of docetaxel resistance in the $A2780_{CBN\rightarrow DXL}$ cell line is comparable to the $A2780_{DXL}$ line. On the other hand, resistance to carboplatin was not significantly reduced in $A2780_{CBN}$ cells after 25 passages (88 days) in the absence of carboplatin ($A2780_{CBN\rightarrow CC}$ cells; p=0.18, Figure 3.6). The results also showed that the IC_{50} for carboplatin of both $A2780_{CBN}$ and $A2780_{CBN\rightarrow DXL}$ cells were significantly higher than that of A2780 parental cells (p=0.03, p=0.03 table 3.4). Therefore, while the $A2780_{CBN\rightarrow DXL}$ cell line acquired docetaxel resistance upon docetaxel exposure and withdrawal from carboplatin (Table 3.3: $A2780_{CBN\rightarrow DXL}$ compared to $A2780_{CBN}$,

p=0.008), the original resistance to carboplatin was not significantly altered (Table 3.4: $A2780_{CBN \rightarrow DXL}$ compared to $A2780_{DXL}$, p=0.19). This suggested that the previous mechanism(s) for carboplatin resistance was retained, even upon acquisition of docetaxel resistance. Alternatively, the newly acquired docetaxel resistance mechanisms also facilitate resistance to carboplatin. To address this issue, the original resistant cell line $A2780_{CBN}$ was continually sub-cultured without any drug to the same passage number of $A2780_{CBN \rightarrow DXL}$ cells. The results (Figure 3.6) showed that the IC_{50} for carboplatin was reduced about 3.6 times in $A2780_{CBN \rightarrow CC}$ cells compared to $A2780_{CBN}$ cells, but the IC_{50} for $A2780_{CBN \rightarrow CC}$ cells was still significantly higher than A2780 parental cells (table 3.7: p=0.013). Taken together, the results suggest that once carboplatin resistance is established in A2780 cells, the resistance phenotype is very stable. Thus, removal of carboplatin from the cells for 88 days, the so called "drug free interval", did not restore their sensitivity. This then suggested that the persistence of carboplatin resistance in $A2780_{CBN \rightarrow DXL}$ cells was independent of the acquisition of docetaxel resistance.

While the $A2780_{CBN \rightarrow DXL}$ and $A2780_{DXL}$ cells share a somewhat similar degree of resistance to docetaxel, the microarray comparison did not identify a common gene profile typical of taxane resistance, for example, changes in drug transporters. However, it is interesting that of the 14 changes in gene expression of 10-fold or more, possibly associated with acquisition of docetaxel resistance in the $A2780_{CBN \rightarrow DXL}$ cell line (Table 3.11), 8 were found in the $A2780_{DXL}$ microarray data. Four of the changes were in the opposite direction in the cell lines, but the other four changes were in the same direction, namely upregulation of expression of the *BEX1*, *HAPLN1*, *SULF1*/*SULF2*, and the *ATP6V0D2* genes (Table 3.11a). The *BEX1* gene is known to play a role in neuronal development, but is widely expressed in other tissues, including in breast cancer. *BEX1* is considered to be a tumour suppressor and has been shown to overcome imatinib

resistance [161]. The *HAPLN1* gene encodes the Hyaluronan and proteoglycan link protein 1, which is expressed in ovarian granulosa cells and facilitates cell survival [187]. *HAPLN1* is also upregulated in metastatic cancer cell lines and tumours, where it promotes Extracellular Matrix (ECM) development, which can contribute to drug resistance. *SULF1* expression was found upregulated in the $A2780_{CBN \rightarrow DXL}$ cell line (18.36 fold) and *SULF2* in the $A2780_{DXL}$ line (2.66) [188,189]. Both *SULF1* and *SULF2* are arylsulfatases which can desulfate heparin sulfate proteoglycans in the ECM [190]. While *SULF1* and *SULF2* appear to have similar enzymatic properties the biological outcomes of their signaling are opposite. *SULF 1* has anti-tumourigenic properties but has been shown to affect cisplatin resistance in ovarian cancer, while *SULF2* appears to play a tumourigenic role, promoting tumour growth in several cancer types [191]. Finally, the *ATP6V0D2* gene codes for a proton pump that protects cells against external acidosis, a common feature of solid tumours, which can stimulate cellular adaptations to promote survival [192,193]. While all these genes do not immediately appear to have a direct link to taxane resistance, they all affect cell growth and survival which may ultimately contribute to the survival of $A2780_{CBN \rightarrow DXL}$ cells during exposure to docetaxel (in addition to drug transporters and other genes that already have altered expression in $A2780_{DXL}$ cells).

Previous microarray data (Table 3.13) suggested that down-regulation of *ANXA1* gene expression (104-fold) and up-regulation of *CDH7* (2.8-fold), *GCLC* (8.5-fold), *GSTO1* (2.4-fold) and *PARP9* (9.4-fold) expression were associated with the acquisition of carboplatin resistance in A2780 cells [150]. Interestingly, there was no difference in the expression of these genes between $A2780_{CBN}$ cells and either $A2780_{CBN \rightarrow DXL}$ cells or $A2780_{CBN \rightarrow CC}$ cells ($p < 0.001$), except for *GCLC*, whose expression in $A2780_{CBN \rightarrow DXL}$ cells was 2-fold lower compared to $A2780_{CBN}$ cells ($p = 8.65 \times 10^{-5}$). This may indicate that down regulation of *ANXA1* and

upregulation of *CDH7, GSTO1* and *PARP9* are important for retention of carboplatin resistance, while *GCLC* may not be.

The *CDH7* gene encodes for Cadherin 7, a calcium-dependent phospholipid-binding protein [194]. *CDH7* plays a role in cell adhesion. Its relevance to cancer resistance is not well known. PARP9 gene encodes for Poly-ADP-ribose polymerase family member 9 and it functions to catalyze addition of ADP-ribose moieties to substrate protein [195]. *PARP9*, a.k.a *BAL1*, has been shown to participate in the DNA repair pathway initiated by *PARP1*, which suggests that upregulated *PARP9* in the $A2780_{CBN}$ and $A2780_{CBN \rightarrow DXL}$ cell lines could contribute to DNA repair, a known mechanism of resistance to carboplatin [196]. The *ANXA1* gene product Annexin I belongs to the annexin family of Ca^{2+}-dependent phospholipid-binding proteins [197]. It is preferentially located on the cytosolic face of the plasma membrane and has phospholipase A2 inhibitory activity. It has been reported that down-regulated *ANXA1* expression contributes considerably to drug resistance in erythroleukemia K562 cells line [198]. When *ANXA1* is silenced or lost in cancer, cells are more prone to DNA damage, suggesting an unidentified diverse role in genome maintenance or integrity [199].

The *GCLC* gene product (Gamma-glutamylcysteine synthetase) functions as rate-limiting enzyme involved in glutathione synthesis [200], while the *GSTO1* gene product is a specific isoform (omega 1) of Glutathione S-transferase (GST). Glutathione is an important antioxidant in plants, animals, fungi and some bacteria and archaea, preventing damage to important cellular components caused by reactive oxygen species (ROS) such as free radicals and peroxides [122–124,126]. The GSTs are a family of isoenzymes. Their best known function is to catalyze the conjugation of the reduced form of glutathione (GSH) to xenobiotic substrates for the purpose of drug detoxification [127]. There is a growing body of evidence supporting the role of GST,

particularly *GST-P*, in cancer development and chemotherapeutic resistance and *GSTO1* likely plays a similar role [201].

Using the same approach as described above (Chapter 2 Materials and Methods 2.2), we were able to select $A2780_{DXL}$ cells for resistance to carboplatin (Fig 3.4): the $A2780_{DXL\rightarrow CBN}$ cell line. The IC_{50} of $A2780_{DXL\rightarrow CBN}$ cells for carboplatin was 24 times higher than that of $A2780_{DXL}$ cells (Figure 3.4, t-test, p=0.0002). In contrast, there was no significant difference between the $A2780_{DXL\rightarrow CBN}$ and $A2780_{CBN}$ cell lines in terms of their IC_{50}s for carboplatin. Resistance to docetaxel, however, was reduced 135 times after long term incubation in the absence of docetaxel (29 passages, 102 days), i.e. upon comparison of the docetaxel sensitivity of $A2780_{DXL\rightarrow CC}$ cells and $A2780_{DXL}$ cells (t-test, p=0.03). Interestingly, the IC_{50} for docetaxel in $A2780_{DXL\rightarrow CBN}$ cells was 3.6 times higher than that of A2780 parental cells but there was no significant difference in docetaxel sensitivity between the two cell lines (t-test, p=0.2). Therefore, the above results indicated that resistance to carboplatin was achieved in the $A2780_{DXL\rightarrow CBN}$, with a concomitant restoration of docetaxel sensitivity.

It should also be noted that docetaxel resistance was also significantly decreased in $A2780_{DXL\rightarrow CC}$ cells when compared to $A2780_{DXL}$ cells (p=0.03), but the IC_{50} for docetaxel in $A2780_{DXL\rightarrow CC}$ cells (550.2 ± 0.29 nM) cells was higher than that of $A2780_{DXL\rightarrow CBN}$ cells (1.76 ± 0.81 nM). Our results thus suggest that the degree of restoration in docetaxel sensitivity was greater upon selection for carboplatin resistance than by simply removing docetaxel selective pressure. Previous microarray data (Table 3.15 $A2780_{DXL}$ vs. A2780) suggested that docetaxel resistance in $A2780_{DXL}$ cells was highly related to down-regulated expression of *CYP1B1* (38-fold) and up-regulated *ABCB1* (34-fold) and *ABCB4* (141-fold) expression. Consistent with their roles in docetaxel resistance, we observed that the expression of these genes changed in the

opposite direction upon selection for carboplatin resistance ($A2780_{DXL\rightarrow CBN}$ vs. $A2780_{DXL}$ cells) or upon elimination of docetaxel selective pressure ($A2780_{DXL\rightarrow CC}$ vs. $A2780_{DXL}$). *CYP1B1* is a member of the cytochrome P450 family (isoform 1B1) [202]. It is a phase 1 drug metabolizing enzyme, which was found to be heavily over-expressed in ovarian cancer cells compared to normal ovary tissue [203]. It has been proposed to be a leading cause of resistance of cancer cells to cytotoxic drugs, including both platinating agents and taxanes [204]. Interestingly, it is thought that resistance to docetaxel associated with *CYP1B1* over-expression may be due to Cyp1b1's ability to bind docetaxel (not to break it down), thereby reducing the amount of active drug in tumour cells [205]. However, since the expression of *CYP1B1* was found to be down-regulated in the $A2780_{DXL}$ cell line in a previous study [186], it is possible that inhibiting taxane detoxification by Cyp1b-mediated metabolism also played a role in docetaxel resistance in A2780 ovarian tumour cells. In Sissung *et al.* [204], a different role for Cyp1b1 in resistance to taxanes was suggested. Cyp1b can oxidize estrogen and the oxidized estrogen metabolite inhibits tubulin polymerization. In this scenario, low levels of Cyp1b would restore tubulin polymerization and allow cells to proliferate. This may explain how reduced expression of CYP1B1 can contribute to resistance to taxanes. CYP1B1 expression is significantly down regulated in the $A2780_{DXL}$ line according to S. Armstrong *et al.* [150]. Further experiments augmenting or reducing Cyp1b1 protein expression in wildtype and docetaxel-resistant A2780 cells, respectively, should be conducted to test the relationship between Cyp1b1 expression and docetaxel sensitivity. Immunoblotting procedures or *CYP1B1* transcript quantitation by qPCR could then be used to determine whether Cyp1b1 expression truly affects docetaxel sensitivity in ovarian tumour cells. Data presented in this thesis indicated that the fold difference in *CYP1B1* expression between $A2780_{DXL\rightarrow CBN}$ and $A2780_{DXL}$ is 67 ($p=7.2 \times 10^{-5}$), which is greater than the 6.0-fold elevation in

CYP1B1 expression found in $A2780_{DXL\rightarrow cc}$ cells compared to $A2780_{DXL}$ cells ($p=4.34 \times 10^{-6}$). This suggests that the greater restoration of docetaxel sensitivity may be related to a greater elevation in *CYP1B1* expression.

The *ABCB1* and *ABCB4* genes code for ATP-binding cassette (ABC) transporter subfamily members B1 and B4, which are multidrug transporters that mediate the ATP-dependent efflux of a variety of chemotherapy drugs from tumour cells [137,206]. Several ABC transporters (such as Abcb2, Abcb1, Abcc1, Abcc2, Abcc4, and Abcg2) have been found to be overexpressed in cell lines selected for resistance to chemotherapy drugs [207–210]. Human Abcb1 (MDR1/P-gp) is one of the most widely studied transporters in drug resistance, and has been implicated not just in resistance to anti-cancer drugs but numerous other drugs as well [211]. Therefore, *ABCB1* and *ABCB4* up-regulation likely played a role in the observed docetaxel resistance found in $A2780_{DXL}$ cells by Armstrong *et al.* [150]. Consistent with this view, we observed that *ABCB1* and *ABCB4* expression were down-regulated 28- and 131-times, respectively, in $A2780_{DXL\rightarrow CBN}$ cells, which could account for the restoration in docetaxel sensitivity. A previous study showed that *in vitro* selection of cells resembles the *in vivo* acquisition of the MDR phenotype, but resistant cells have to be cultured under constant selective pressure to ensure a stable phenotype [212]. The downregulation of *ABCB1* expression seen in our microarray data would help explain the loss of docetaxel resistance in $A2780_{DXL\rightarrow CBN}$ cells, as seen in our clonogenic studies. According to microarray data (Table 3.15), *ABCB1* and *ABCB4* are both downregulated upon selection of $A2780_{DXL}$ cells for carboplatin resistance (27.8 fold and 130 fold, respectively) or upon removal of docetaxel selective pressure ($A2780_{DXL\rightarrow CC}$ cells; 14.73 fold and 9.25 fold, respectively). This suggests that greater suppression of Abcb1 and Abcb4 expression is associated with greater loss of docetaxel resistance loss. Moreover, selection for carboplatin

resistance induces a greater downregulation in the expression of these drug transporters than simply eliminating docetaxel selective pressure.

While our clonogenic assays confirmed the establishment of docetaxel resistance in the $A2780_{CBN \rightarrow DXL}$ cells, no change in the expression of *CYP1B1*, *ABCB1* and *ABCB4* was observed upon acquisition of docetaxel resistance to create the $A2780_{CBN \rightarrow DXL}$ cell line (Table 3.11). As the original carboplatin resistance persists in the $A2780_{CBN \rightarrow DXL}$ cells, it appears to be a dual drug resistant cell line (resistant to both carboplatin and docetaxel). This may account for the gene expression differences between the original $A2780_{DXL}$ cell line and $A2780_{CBN \rightarrow DXL}$ cells, both of which exhibit docetaxel resistance. Since the dual drug resistant cell line $A2780_{CBNDXL}$ has been established previously, it might be valuable to compare differences in gene expression between $A2780_{CBN \rightarrow DXL}$ and $A2780_{CBNDXL}$ cells in microarray studies. To investigate the mechanisms behind drug resistance, microarray analysis was performed, comparing gene expression between $A2780_{CBN}$-variants (Table3.3) and $A2780_{DXL}$-variants (Table 3.4). Based on clonogenic assay data, carboplatin resistance was established and original docetaxel resistance was lost in $A2780_{DXL \rightarrow CBN}$ cells; docetaxel resistance was also lost in $A2780_{DXL \rightarrow CC}$ cells. Thus, differences in gene expression between $A2780_{DXL \rightarrow CBN}$ cells and $A2780_{DXL}$ cells would be expected to be associated with the acquisition of carboplatin resistance and/or the loss of docetaxel resistance. In contrast, differences in gene expression between $A2780_{DXL \rightarrow CC}$ vs $A2780_{DXL}$ would likely be related to loss of docetaxel resistance only. We thus hypothesized that genes in common between the two groups would represent genes associated with loss of docetaxel resistance, while the unique genes within the two sets would more likely to be related to carboplatin resistance establishment (Table 3.5)

Among 8 notable gene expression changes associated with selection of $A2780_{DXL}$ cells for resistance to carboplatin, *BEX1, CYB5A, CYB5R2,* and *FAS* were down-regulated, while *BCL6*, *SLC25A24*, *PIX2* and *EMP1* were up-regulated. *BEX1* was down-regulated 138 times when the $A2780_{DXL \rightarrow CBN}$ cell line was established. A study in 2009 demonstrated that the gene for brain expressed X-linked 1 protein (*BEX1*) was silenced in secondary imatinib-resistant human erythroleukemia K562 cell line [213] . Re-expression of *BEX1* in this cell line restored imatinib sensitivity, resulting in the induction of apoptosis [213].

The *BCL6* gene was up-regulated 15.5 times in $A2780_{DXL \rightarrow CBN}$ cells (table 3.14: $p=3.82 \times 10^{-4}$). The protein encoded by *BCL6* gene is an evolutionarily conserved zinc finger transcription factor. It acts as a sequence-specific repressor of transcription [163]. Overexpression of *BCL6* in mouse C2C12 myocytes enhanced cell viability by preventing apoptosis. High levels of Bcl6 antisense mRNA expression induced apoptosis during the differentiation of C2C12 cells, but this was effectively prevented by infection with an adenovirus that expressed a Bcl6 sense mRNA [164]. Another study by the same research group also reported that *BCL6* overexpression significantly inhibited apoptosis caused by etoposide. *BCL6* overexpression was found to inhibit the increase in ROS levels and apoptosis in response to etoposide and other chemotherapeutic reagents [162].

CYB5A and *CYB5R2* code for cytochrome b5 type A and cytochrome b5 reductase 2 respectively. Both of the two genes were down-regulated 25.5 (Table 3.14 $p=1.23 \times 10^{-4}$) and 10 times (Table 3.14 $p=1.09 \times 10^{-5}$), respectively, after carboplatin resistance establishment in $A2780_{DXL \rightarrow CBN}$ cells. Cytochrome b5 is a membrane bound hemoprotein which functions as an electron carrier for several membrane bound oxygenases [214]. A significant correlation was seen between shorter survival and loss of the 18q22.3 in the highly invasive and resistant cells of

pancreatic cancer. Further investigation revealed that CYB5A had a prognostic value in metastatic patients [215]. Moreover, both *in vitro* and *in vivo* studies clarified a role for CYB5A in inhibiting the activity of oncogenic phenotypes through induction of a well-known survival pathway in tumor cells (autophagy) [165,166].

SLC25A24 was found to be up-regulated 794-fold in $A2780_{DXL \rightarrow CBN}$ cells compared to $A2780_{DXL}$ cells (table 3.14 $p=7.6x10^{-5}$). The gene is a member of the mitochondrial carrier subfamily of solute carrier protein genes. The product of this gene, solute carrier family 25 member 24, functions as a gated pore that translocates ADP from the cytoplasm into the mitochondrial matrix and ATP from the mitochondrial matrix into the cytoplasm [167]. The protein forms a homodimer embedded in the inner mitochondria membrane [168,169]. It has been shown that suppressing the expression of this gene induces apoptosis and inhibits tumour growth. *SLC25A24* has been listed as one of several chemo-resistance genes in a previously published microarray study [186]. 10 human tumour cell lines, including parental cells and resistant sub cell lines selected for resistance against doxorubicin, melphalan, teniposide and vincristine were studied [216–218].

The *FAS* gene encoding the Fas receptor (FasR) was down-regulated 11-fold as carboplatin resistance was established in the docetaxel resistant cell line (t-test, $p=1.23 \times 10^{-5}$). The Fas receptor is a death receptor on the surface of cells that leads to programmed cell death, which is one of two regulated apoptotic pathways [170,219]. Binding of Fas ligand (FasL) to Fas receptor (FasR) induces trimerization of FasR, which recruits caspase-8. The oligomerization of caspase-8 may result in self-activation of proteolytic activity and trigger protease cascade (caspases) [220]. The activated caspases can induce apoptosis, resulting in the cleavage of various substrates, such as poly-ADP-ribose polymerase (PARP), lamin, rho-GDI, and actin, and the induction morphological changes to the cells and nuclei [221,222].

PITX2 was up-regulated 220-fold when carboplatin resistance was established in the $A2780_{DXL}$ cell line. The protein encoded by the *PITX2* gene, Pitx2, acts as a transcription factor. It is responsible for the asymmetrical development of the heart, lungs, spleen, and the eyes [223]. Pitx2 is over-expressed in many cancers [224–227]. Increased expression of the Pitx2 transcription factor has been found in ovarian cancer cells when compared to noncancerous cell lines [224]. In renal cancer, Pitx2 regulates expression of *ABCB1* by binding to the promoter region of *ABCB1*. Therefore, increased expression of *PITX2* in renal cancer cells is associated with increased expression of Abcb1 and so have a greater resistance to chemotherapeutic agents [225]. Other studies have shown that *PITX2* is also overexpressed in human esophageal squamous cell carcinoma (ESCC) compared to normal esophageal squamous cells and greater expression of Pitx2 is positively correlated with clinical aggressiveness of ESCC [226]. However, in the $A2780_{DXL \rightarrow CBN}$ cell lines, docetaxel resistance is not elevated. This is further confirmed by the downregulation of *ABCB1* (Appendix V). This might mean the protein level of Pitx2 is not correlated with gene *PITX2*, which need to be confirmed by western blot. On the other hand, the correlation between carboplatin resistance and *PITX2* remains to be studied.

The *EMP-1* gene was up-regulated 506 times in $A2780_{DXL \rightarrow CBN}$ cells compared to $A2780_{DXL}$ cells. Interestingly, the expression of its gene product (a surface biomarker) was found to be correlated with gefitinib resistance [228]. *EMP-1* expression was further correlated with the complete lack of response or partial response to gefitinib in lung cancer patient samples, as well as clinical progression to secondary gefitinib resistance [229]. This report thus suggests a role of the adhesion molecule, Emp-1, as a biomarker of gefitinib clinical resistance, and further suggests a probable cross-talk between this molecule and the EGFR signaling pathway [229,230].

Based on the above information and our microarray gene profiling experiments (table 3.15), most of the highlighted changes in gene expression upon selection for carboplatin resistance coded for proteins that protect cells from death by inhibiting apoptotic pathways. Therefore, inhibited apoptotic cell death may be one of the major mechanisms behind acquired carboplatin resistance in $A2780_{DXL\rightarrow CBN}$ cell lines. However, this needs to be confirmed using various tools that can monitor apoptosis induction and resistance.

As we discussed above, acquired carboplatin resistance in $A2780_{DXL\rightarrow CBN}$ cell line may be caused by inhibiting apoptosis. While carboplatin resistance was established in $A2780_{DXL\rightarrow CBN}$ cells, the existing resistance to docetaxel was lost or partially lost in the cell line. There is thus some restoration of docetaxel sensitivity in $A2780_{DXL\rightarrow CBN}$ cells (Fig 3.5). The next question is why the same changes in gene expression that inhibit carboplatin-induced apoptosis could permit cell death via docetaxel? It is well known that carboplatin can act as a DNA crosslinker [24,29,231]. It damages DNA, induces DNA repair and, ultimately induces apoptosis [232,233]. Enhanced DNA repair and downregulated apoptotic pathways are main mechanisms for the resistance to carboplatin [216,234–236]. On the other hand, taxanes target microtubules and cause mitotic arrest in the cells [217,218] . The mechanism of resistance to taxanes is mainly associated with increased drug efflux by ABC (ATP binding cassette) transporter family, especially Abcb1 (Chapter 1.3.4) [218,237]. In agreement with reported mechanism of resistance to taxanes, our results on microarray analysis (table 3.14) show that *ABCB1* gene is down-regulated 28 times and *ABCB4* is down-regulated 131 times in $A2780_{DXL\rightarrow CBN}$ cell line comparing to $A2780_{DXL}$ cell line. This strongly suggests that decreased docetaxel efflux from cells is one of the main reasons for docetaxel resistance lost in $A2780_{DXL\rightarrow CBN}$ cell line. As the result of decreased the drug efflux, there would be higher amounts of docetaxel accumulated in the cells while treating cells with docetaxel and

therefore higher cytotoxicity is observed. The reduction in *ABCB1* expression would not enable more carboplatin accumulation in $A2780_{DXL \rightarrow CBN}$ cells, since carboplatin is not a substrate for the Abcb1 transporter. A study has also suggested that high concentrations (0.2-30 M) of docetaxel can upregulate pro-apoptotic factor Bak and Bax and downregulate anti-apoptotic factor Bcl-X_L [75]. Therefore apoptotic pathways contributing to docetaxel cytotoxicity may actually promote carboplatin resistance or *vice versa*. However, this hypothesis must be confirmed by future experimentation.

In our study, the $A2780_{DXL \rightarrow CBN}$ cell line acquired resistance to carboplatin, while existing docetaxel resistance was partially to fully lost. These findings support my hypothesis that sequentially exposing cells to a second drug permits restoration of sensitivity to the first drug to a greater extent than by simply removing exposure to docetaxel (selective pressure). However, the establishment of the $A2780_{CBN \rightarrow DXL}$ resulted in retention of the original carboplatin resistance. This suggests that carboplatin resistance was established by a mechanism independent of the establishment of docetaxel resistance. Similarly, during the so-called "drug free interval", carboplatin resistance also stably persisted in the cells ($A2780_{CBN \rightarrow CC}$), while docetaxel sensitivity can be partial to fully restored ($A2780_{DXL \rightarrow CC}$).

$A2780_{CBN \rightarrow DXL}$ (or $_{CC}$)	carboplatin resistance <u>remains</u>
$A2780_{DXL \rightarrow CBN}$	carboplatin resistance <u>established</u>
$A2780_{DXL \rightarrow CBN}$ (or $_{CC}$)	docetaxel resistance is lost
$A2780_{CBN \rightarrow DXL}$	docetaxel resistance established

It appears that resistance to carboplatin is less reversible than docetaxel, meaning resistance to carboplatin may be a more stable phenotype (once achieved), while resistance to docetaxel is more "transient" and "reversible".

Permanent stable chromosomal alterations can take place, which are not easily reversed. This may particularly be the case for DNA damaging agents, such as cisplatin or carboplatin, compared to taxanes, although chromosomal alterations are also observed upon acquisition of docetaxel resistance (Reed et al., Epigenetics. 2008 Sep;3(5):270-80). A research group has provided evidence for alterations in gene copy number as a mechanism for chemo-resistance. They conducted molecular cytogenetic analysis of 23 chemo-resistance cancer cell lines, 8 of which were cisplatin resistant cell lines. Among those altered genes, 13 genes belong to ABC family and anti-apoptotic BCL-2 was consistently increased [238].

BRCA1/2-deficient cancer cells are hypersensitive to DNA-crosslinking agents including cisplatin. Previous studies have shown that acquired cisplatin resistance can be mediated by secondary intragenic mutations in *BRCA2* that restore the wild type *BRCA2* reading frame in ovarian and breast carcinoma [239–241]. Therefore, some of carboplatin resistance in the cell line may be caused by chromosomal alterations if the damage is permanent, then it would be non-reversible. Glutathione and GST are related to detoxification of platinating agents. Another study confirmed at the genetic level that Glutathione S Transferase-π copy number is amplified when cells develop cisplatin resistance [127].

These interesting phenomena may help provide guidance on approaches to improve clinical treatment for ovarian cancer patients using chemotherapy. Carboplatin/docetaxel combination chemotherapy is now the standard regimen in the treatment of ovarian cancer. Acquired

resistance to both agents will be established in most ovarian cancer cells after a period of treatment. However, as suggested by current study, the sensitivity to docetaxel can be partially or fully restored, if not co-administered with a platinating agent. Therefore, docetaxel may be subsequently readministered after a certain "drug free interval", in particular after carboplatin treatment. Thus, repeated sequential administration of docetaxel and carboplatin may lengthen the duration of useful clinical response than a single co-administration of the two agents. This could be assessed in clinical trials, providing the planned regimen can be expected to provide an equivalent or superior level of clinical response with equivalent or less toxicity.

In this thesis, we have also documented the changes in gene expression, which accompany loss of previously established drug resistance with or without acquisition of resistance to a new chemotherapy agent. However, more experiments need to be conducted to assess the relevance of these changes in gene expression in the above-described alterations in drug sensitivity. Confirmation of the changes in gene expression could be obtained by qPCR and western blotting experiments. Moreover, even if confirmed at the transcript or protein levels, post-transcriptional and post-translational events may ultimately impact on gene expression and drug sensitivity, for example, through the production of a non-coding RNAand/or the production of miRNAs. In addition, splicing variants are possible that would not be detected by microarrays [242,243]. Ultimately, we will then have to evaluate the clinical relevance of our findings through *in vivo* studies.

This could involve simulations of the *in vivo* microenvironment or animal experiments. There are a lot of models to simulate the *in vivo* microenvironment, including multicellular tumour spheroids [244], multi-layered cell culture (MCC) on a permeable membrane support [97,245]. In

animal tests, solid tumours can be transplanted into animal bodies to immerse in microenvironment.

Finally, the above cultured cell lines represent a large collection of stable clones of cells surviving after selection and do not represent selection for a single clone of surviving cells that is subsequently propagated. Therefore, it is unlikely that the differences observed between the various cell lines represent clonal variation in the cellular population.

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Appendices

Appendix I Gene Expression Changes in $A2780_{CBN-DXL}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
TP6V0D2	35.6	SLC16A3	4.79	GRB14	3.82	RASSF5	3.27
SLITRK6	21.7	MID1	4.75	FBXO15	3.79	MT2A	3.26
MECOM	20.3	CYB5A	4.72	THC2575678	3.76	DLGAP5	3.24
MUC15	18.7	SCHIP1	4.68	USP18	3.71	EEF1A2	3.23
SULF1	18.3	BHLHE41	4.66	NUP210	3.60	ENST00000531488	3.23
HAPLN1	17.1	KCTD19	4.55	C21orf58	3.59	SIPA1	3.23
ATP6V0D2	17.0	CA2	4.47	A_32_P75141	3.59	KIAA0101	3.23
PRL	16.6	AS3MT	4.46	IGFLR1	3.58	CASC5	3.22
PDGFRA	16.1	FILIP1L	4.41	MAP2K6	3.58	PPFIA4	3.21
PRR16	15.9	CSRP2	4.40	A_24_P49657	3.58	LOC100507303	3.21
PLAC8	15.9	HMMR	4.40	GPER	3.58	TCF4	3.21
BEX1	15.5	THC2731337	4.37	DNAJC22	3.53	WNT3A	3.21
RND3	15.3	GLYATL1	4.36	RAD54B	3.52	MCF2L	3.21
SPON2	12.7	FAM198B	4.34	BDH2	3.51	MYLK	3.20
PLEKHG4	9.81	RAB3D	4.30	SPC24	3.50	TRIM6	3.19
FES	8.53	THC2770932	4.26	FOXN4	3.49	KIF11	3.18
KLHDC9	8.15	PLA2G16	4.22	DDB2	3.47	C18orf56	3.18
IGFBP5	8.05	AK054718	4.20	ANK1	3.46	FBXL5	3.17
THC2493376	7.40	BMF	4.19	MCAM	3.43	HRSP12	3.13
NTS	7.14	PLEKHA2	4.17	ITPKB	3.43	HEYL	3.12
DNAJC15	6.82	CGNL1	4.17	DNMT3B	3.43	MT1E	3.12
PBX1	6.69	IKZF2	4.16	ENST00000432751	3.42	KIAA0586	3.12
RASSF4	6.54	BAIAP2L2	4.12	MT2A	3.42	C1orf21	3.11
ARID5B	6.31	CT45A1	4.09	LOC729887	3.40	GREB1	3.10
FGF18	6.23	TNS3	4.06	ENST00000551187	3.37	LRRCC1	3.08
PACSIN1	6.11	NMU	3.99	MT1X	3.36	SIPA1L2	3.08
DCN	5.76	BCHE	3.96	FAM183B	3.35	OLFML3	3.06
POU4F1	5.64	TGFB3	3.96	KIF14	3.34	C9orf100	3.06
STAU2	5.62	USP18	3.92	LOC100652730	3.34	MCF2L-AS1	3.04
PBX1	5.45	RNF213	3.92	BC037328	3.33	MIS18BP1	3.03
THC2707492	5.30	CCDC116	3.92	PRR11	3.33	SHROOM2	3.03
ENST00000502419	5.28	HSBP1L1	3.88	DFNB31	3.32	NGEF	3.02
KRT222	5.11	CORO2A	3.88	C16orf74	3.32	THC2699069	3.02
ENST00000428928	4.96	FBLN5	3.85	MT2A	3.31	PRIM1	3.02
DPYSL5	4.94	LOC100505679	3.85	RBM43	3.30	KIAA0586	3.02
EOMES	4.90	SYCP2	3.84	CDH10	3.29	ADAMTS3	3.01
CDKL5	4.86	A_23_P66347	3.83	BUB1	3.29	RAD54B	3.01
RBM43	4.81	OCA2	3.82	LXN	3.28	EFCAB11	3.00
GPR162	4.80	SYCP2	3.82	ENST00000375678	3.27	GLRX	2.99

Appendix I Gene Expression Changes in $A2780_{CBN-DXL}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
MTL5	2.99	CCDC109B	2.80	G2E3	2.66	JMJD7	2.49
MTMR9LP	2.98	HMGN5	2.80	GPSM2	2.65	SGOL1	2.49
WDHD1	2.98	CASC5	2.80	GKAP1	2.65	ESPL1	2.48
PLK1	2.97	TMEM107	2.79	RFC3	2.65	SLC25A40	2.48
MT1L	2.96	ESCO2	2.77	DIP2A	2.64	SIX4	2.48
TRERF1	2.95	NDC80	2.77	THC2694800	2.64	PTTG3P	2.48
PBK	2.94	FZR1	2.76	CXorf57	2.63	POLE2	2.48
C20orf96	2.92	ANKRD45	2.76	A_32_P65157	2.62	USP41	2.46
KIAA1147	2.92	SNX5	2.76	BTN2A2	2.62	LOC100127983	2.46
STYX	2.92	RAB3IP	2.76	E2F8	2.61	THC2753400	2.45
TRIM6	2.92	TPM1	2.75	THC2676635	2.61	GCHFR	2.45
A_24_P230009	2.91	THC2538534	2.75	A_24_P409440	2.61	LMO7	2.45
THRA	2.91	KIF20A	2.75	A_24_P84711	2.59	DLAT	2.45
TBC1D23	2.91	CCNB2	2.75	OSR2	2.59	RCAN3	2.45
NFE2	2.91	TBXA2R	2.75	TPMT	2.58	A_32_P2303	2.45
DHRS3	2.91	DEPDC1	2.74	RASGRP2	2.57	RPL22L1	2.45
MT1X	2.91	LRRCC1	2.74	ENST00000452565	2.57	PIF1	2.45
NUP210	2.90	TMEM65	2.74	LOC145757	2.56	TK1	2.44
SRPX	2.90	TMEM19	2.74	TPMT	2.56	C1orf106	2.44
LOC100505932	2.90	TMC6	2.73	A_23_P72014	2.56	LOC389493	2.44
ALDH1A3	2.89	IFI30	2.73	BU602485	2.56	HMGB2	2.44
CRIP2	2.89	ABCA1	2.73	LOC644656	2.56	ABCC6	2.44
C5orf39	2.88	IKBKE	2.73	CABYR	2.56	BIRC5	2.43
THC2677011	2.88	CDCA2	2.72	FAM120C	2.55	ZNF323	2.43
NEK2	2.87	MT1H	2.72	NEK2	2.55	CHEK1	2.43
CENPF	2.86	OLFML3	2.72	PTTG2	2.54	TRERF1	2.42
BC032755	2.86	CARD8	2.72	KIF15	2.54	CCDC24	2.42
STMN3	2.85	CORO2A	2.71	PHF15	2.53	ANXA11	2.42
TBC1D23	2.84	IKZF2	2.71	LOC100289361	2.53	MELK	2.42
AMOT	2.84	ABLIM1	2.71	MYLK	2.53	TMEM37	2.41
C2CD4C	2.83	STAU2	2.69	A_32_P182135	2.52	ALDH6A1	2.41
TMEM106C	2.83	FANCI	2.68	BOLA1	2.52	UBE2H	2.40
C19orf51	2.82	NDC80	2.68	PTPRF	2.52	GHR	2.40
ATAD2	2.82	A_23_P392897	2.68	CENPF	2.51	AATK	2.39
STK33	2.82	PPM1F	2.68	SPAG5	2.51	ENO3	2.39
MIS18BP1	2.82	A_24_P178475	2.67	ARL6IP5	2.51	DEPDC1B	2.39
CKMT1A	2.81	LOC100240734	2.67	SPC25	2.50	TMEM107	2.38
COMTD1	2.80	CAND2	2.67	CRISPLD1	2.50	DLG3	2.38
CIT	2.80	E2F7	2.67	RBM20	2.50	F11R	2.38

Appendix I Gene Expression Changes in $A2780_{CBN-DXL}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
FAM198A	2.38	PACSIN1	2.31	A_32_P121674	2.24	TP53I3	2.17
JUP	2.38	OIP5	2.31	TPD52	2.24	NCAPG	2.17
CENPI	2.38	AKR1B1	2.31	WNK2	2.23	MFSD3	2.17
BORA	2.38	BC018626	2.31	NCAPG2	2.23	TSPAN7	2.17
FBXO4	2.38	ARRB1	2.31	PECR	2.23	ANXA11	2.17
THC2732175	2.38	LOC100131170	2.31	GPC4	2.22	A_32_P174385	2.16
THC2656479	2.37	DERA	2.31	PCBD2	2.22	MCF2L	2.16
PTTG1	2.37	SPEG	2.31	MT1B	2.22	HIP1	2.16
HIP1	2.37	HIBCH	2.31	GLDC	2.22	ELL3	2.16
HIST1H4C	2.37	CCNA2	2.31	ALDH4A1	2.22	RAB3B	2.16
FOXM1	2.37	MFSD4	2.30	SUMO3	2.21	PCNT	2.15
UBR7	2.36	DZIP3	2.30	BM458245	2.21	NUF2	2.15
NDRG2	2.36	CLGN	2.30	TRIM45	2.21	STRADB	2.15
CDKN3	2.36	HBQ1	2.29	TMEM126A	2.21	CCDC80	2.15
C10orf76	2.36	AURKB	2.29	PHF19	2.21	LOC100507475	2.15
ATL3	2.36	PRDM15	2.29	RDM1	2.21	GRIN2C	2.15
ZNF695	2.36	SHMT1	2.29	C21orf119	2.20	POLR3GL	2.15
TMEM187	2.35	A_24_P323682	2.29	KIAA0182	2.20	AIM1L	2.15
HIST1H4B	2.35	HIST1H1B	2.28	MOK	2.20	TTK	2.14
ANLN	2.35	PNKD	2.28	WDHD1	2.20	A_24_P178167	2.14
PI4K2B	2.35	PRIM2	2.28	PRKCH	2.20	APOBEC3F	2.14
PSRC1	2.35	BQ933774	2.28	LRR1	2.20	THC2517184	2.14
PPPDE1	2.34	C9orf40	2.27	THC2689749	2.20	CKAP2L	2.14
UCHL5	2.34	ZNF197	2.27	MCM3AP-AS1	2.19	C16orf55	2.14
HIST1H4L	2.34	FLOT2	2.27	RAD51AP1	2.19	C12orf48	2.13
DEPDC1	2.34	FDXR	2.27	RRM1	2.19	SMC2	2.13
C14orf93	2.33	STAU2	2.27	ENST00000494075	2.19	CARHSP1	2.13
TNNI3	2.33	APOBEC3B	2.26	KIF18A	2.18	A_32_P760762	2.13
STRADB	2.33	TET1	2.26	PKN3	2.18	FAM82B	2.13
RNFT2	2.33	TBC1D5	2.26	SH2D4A	2.18	AK094175	2.12
MSI2	2.33	ENST00000456688	2.26	IGFBP2	2.18	SLC2A4RG	2.12
LMCD1	2.33	B3GNT1	2.25	SALL2	2.17	WNT3	2.12
RAD51C	2.32	PERP	2.25	STARD8	2.17	ATXN3	2.12
LOC100506054	2.32	OXCT1	2.25	DISP2	2.17	HIRIP3	2.12
ENST00000521696	2.32	CALM1	2.24	AK1	2.17	SLC39A4	2.12
FBXO16	2.32	ZFHX2	2.24	DZIP3	2.17	DHFR	2.12
UCHL5	2.32	HIST1H4D	2.24	CKLF	2.17	RBBP5	2.12
TESC	2.32	NUSAP1	2.24	MRPL35	2.17	SMYD2	2.12
TFDP2	2.31	DOCK3	2.24	CCDC28B	2.17	PCDH17	2.12

Appendix I Gene Expression Changes in $A2780_{CBN-DXL}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
H2AFJ	2.11	PSMB10	2.06	LRBA	2.02	LOC100133091	-2.02
FKBP3	2.11	MYCBP	2.06	TMPO	2.02	MYOF	-2.02
ECT2	2.11	ENST00000420759	2.06	HSPB1	2.02	C19orf28	-2.02
PDE9A	2.11	C18orf54	2.06	LOC338799	2.02	HIST1H2BH	-2.02
WDR76	2.11	HCFC2	2.06	ZC4H2	2.02	C6orf70	-2.02
AZI1	2.11	ITGB3BP	2.06	RACGAP1	2.02	RAB2A	-2.02
GNG2	2.11	A_24_P92823	2.06	ASRGL1	2.02	ZBTB46	-2.03
PVRL2	2.11	TRIM66	2.05	COLEC12	2.01	RALGDS	-2.03
NCAPH	2.11	INCENP	2.05	NUCKS1	2.01	ACTB	-2.03
ECT2	2.11	A_32_P4608	2.05	CACNB3	2.01	BU903025	-2.03
CENPP	2.11	CEP250	2.05	S100A4	2.01	THC2669419	-2.03
CCDC125	2.10	DKK3	2.05	GRAMD1C	2.01	HLA-B	-2.03
ARL6IP5	2.10	ATP2B4	2.05	CENPA	2.01	STX4	-2.03
LOC100505771	2.10	HSDL2	2.05	RAB8B	2.01	LRP8	-2.03
C14orf33	2.10	LRRC40	2.04	CDC20	2.01	A_24_P161393	-2.03
CDC25C	2.09	ARHGEF16	2.04	TRMT1L	2.01	C18orf8	-2.04
THC2541678	2.09	CKLF	2.04	CCR10	2.00	THC2563307	-2.04
MAPK12	2.09	NUDT1	2.04	CCDC138	2.00	A_24_P76210	-2.04
LSM3	2.09	C6orf226	2.04	GNB4	2.00	RSL1D1	-2.04
MTA3	2.09	CCDC88B	2.04	WDR34	2.00	STK40	-2.04
CTBP1	2.09	CDC45	2.04	PRMT2	2.00	NFKB2	-2.04
A_32_P57002	2.09	SEC22C	2.04	LOC100130331	-2.00	FOXC1	-2.04
TMEM14A	2.09	LOC100506965	2.04	THC2783023	-2.00	A_32_P123589	-2.04
GPR19	2.09	AGPS	2.04	C11orf41	-2.00	MAP3K2	-2.05
CCNG2	2.09	UBR5	2.04	GOT1	-2.00	MALAT1	-2.05
CDCA3	2.09	BPTF	2.04	COQ10B	-2.01	ITPRIPL2	-2.05
DHFR	2.09	GALNTL1	2.04	UFM1	-2.01	HSPA4	-2.05
WDR90	2.08	CFD	2.04	ZNF222	-2.01	A_24_P367100	-2.05
A_24_P281175	2.08	ZNF273	2.03	TPM4	-2.01	CASD1	-2.05
TOP2A	2.08	DHTKD1	2.03	TRIB1	-2.01	HLA-B	-2.05
FANCD2	2.08	DLEU1	2.03	SLC19A2	-2.01	HIST1H2BF	-2.05
RXRA	2.08	DSCC1	2.03	PIGM	-2.01	THC2563568	-2.05
CLEC2D	2.08	ENST00000523354	2.03	BE780682	-2.01	PHF14	-2.05
CKMT1A	2.08	PLBD1	2.03	CYR61	-2.01	PCMT1	-2.05
ANG	2.07	MRE11A	2.03	HIST1H2BL	-2.01	SYT15	-2.05
CCNB1	2.07	GPD2	2.03	ACTG1	-2.01	COL6A2	-2.05
KLHDC8B	2.07	ZWINT	2.03	SLC35E1	-2.02	FAM3C	-2.06
FANCG	2.07	SNHG13	2.02	BC000206	-2.02	UNKL	-2.06
CCDC88A	2.07	CTSL2	2.02	CASK	-2.02	ROR2	-2.06

Appendix I Gene Expression Changes in $A2780_{CBN-DXL}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
HLA-B	-2.06	ACSS2	-2.11	COL3A1	-2.16	BM695552	-2.22
ENST00000330588	-2.06	FAM106A	-2.11	BEND3	-2.16	LOC100133920	-2.22
IFI27L2	-2.06	PITPNA	-2.11	PAQR9	-2.16	SARM1	-2.22
ARHGAP32	-2.06	ME1	-2.11	DNM3OS	-2.16	A_24_P871726	-2.22
A_32_P79719	-2.07	LOC728739	-2.11	S73202	-2.16	RNF145	-2.22
KIAA1919	-2.07	THC2660636	-2.11	AL832534	-2.16	BSN	-2.22
DDX19B	-2.07	KLHDC7B	-2.11	ZNRF1	-2.16	DPH3	-2.23
ST6GALNAC6	-2.07	MSH3	-2.11	WDR19	-2.17	MME	-2.23
PLEKHA4	-2.07	CEP104	-2.12	ELOVL6	-2.17	LPIN1	-2.23
BI256572	-2.07	A_24_P358606	-2.12	KRCC1	-2.17	FAM3C	-2.23
PDCD2	-2.07	A_32_P174374	-2.12	RFTN1	-2.17	LRRTM4	-2.24
TPM4	-2.08	A_24_P49800	-2.12	ATP1B1	-2.17	TULP4	-2.24
HES4	-2.08	B4GALNT1	-2.12	A_32_P161140	-2.18	TAC1	-2.24
A_24_P187626	-2.08	ZNF222	-2.12	ADCY1	-2.18	HIST1H1C	-2.24
C13orf15	-2.08	KLHL2	-2.12	C6orf192	-2.18	CEBPA	-2.24
C6orf120	-2.08	LOC148709	-2.12	MAP9	-2.18	SLC9B2	-2.25
CHRD	-2.08	TIMP1	-2.12	HOPX	-2.18	LOC80054	-2.25
ENST00000485253	-2.08	LPCAT1	-2.13	PRPH	-2.18	ASS1	-2.25
BC049371	-2.08	MBL2	-2.13	LOC100506710	-2.18	NAB2	-2.25
PLEKHA4	-2.08	A_24_P692600	-2.13	GCLC	-2.18	A_24_P306814	-2.25
FTL	-2.08	A_32_P204903	-2.13	ZNF295	-2.19	USP14	-2.25
CRADD	-2.08	RNASET2	-2.13	HSD17B7	-2.19	LARP6	-2.25
TOLLIP	-2.08	HLA-H	-2.13	C16orf52	-2.19	DNAJB9	-2.26
LOC729680	-2.08	RGS1	-2.13	PDCD2	-2.19	ANKRD10	-2.26
CYBRD1	-2.08	ACADVL	-2.13	GBE1	-2.19	MAP9	-2.26
NR2F1	-2.09	MYO1C	-2.14	ZNF26	-2.19	IGF1R	-2.26
A_24_P255786	-2.09	HSD17B7	-2.14	BC041955	-2.20	SFT2D1	-2.26
RBCK1	-2.09	DKFZp761E198	-2.14	A_24_P178444	-2.20	CHPF2	-2.26
TCF15	-2.09	A_24_P152345	-2.14	C19orf28	-2.20	SGK223	-2.27
AF086376	-2.09	MVK	-2.14	ZBTB46	-2.20	ZBTB1	-2.27
HIST1H2AD	-2.09	UGGT2	-2.14	UGCG	-2.20	FAM59A	-2.27
THBS1	-2.09	MALAT1	-2.14	A_24_P578445	-2.20	CEBPA	-2.28
AK4	-2.09	MTHFD1L	-2.15	KLHDC5	-2.20	MVD	-2.28
POTEKP	-2.10	NFE2L1	-2.15	MANEAL	-2.21	CEP104	-2.28
A_32_P78488	-2.10	BC073815	-2.15	MAP3K14	-2.21	SLC7A11	-2.29
HSD17B14	-2.10	C11orf96	-2.15	CRLF1	-2.21	STX4	-2.29
ELOVL5	-2.10	CHPF2	-2.15	HSPA13	-2.21	CHD7	-2.29
A_32_P125185	-2.10	XIST	-2.15	TAGLN	-2.22	NKAIN1	-2.29
ROBO2	-2.10	TPRG1L	-2.15	A_24_P101771	-2.22	AF126109	-2.29

Appendix I Gene Expression Changes in $A2780_{CBN-DXL}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
TRAPPC6A	-2.29	EMP1	-2.38	UFM1	-2.47	HES2	-2.64
UCHL1	-2.29	SLC22A18	-2.38	AK123066	-2.47	EYA4	-2.64
OSTM1	-2.30	CEACAM1	-2.39	A_32_P128399	-2.47	SHC1	-2.64
NIPAL2	-2.30	DUSP8	-2.39	MIR22HG	-2.47	THC2729109	-2.64
AB014766	-2.30	NUS1	-2.39	EFCAB1	-2.47	AK094629	-2.66
EPT1	-2.30	PTPRH	-2.39	A_23_P125109	-2.48	CTGF	-2.67
PURB	-2.30	CU678847	-2.40	SEZ6L2	-2.48	HSPA5	-2.67
BM683477	-2.30	C1S	-2.40	HABP4	-2.48	BC037919	-2.67
STX3	-2.30	KLF13	-2.40	ASPH	-2.48	PABPC4L	-2.68
LOC647979	-2.30	CNKSR3	-2.40	AK130366	-2.49	A_32_P30898	-2.68
SAP18	-2.31	COL3A1	-2.40	TRIM7	-2.49	MYO15A	-2.69
A_24_P660797	-2.31	CLCN6	-2.41	CYP51A1	-2.49	GCLC	-2.69
XBP1	-2.31	GJA1	-2.41	A_23_P57836	-2.49	SOLH	-2.70
FYN	-2.32	RSPH3	-2.41	CYCS	-2.50	MGAT5B	-2.71
ITPRIPL2	-2.32	NUPL1	-2.41	THC2734788	-2.50	OGT	-2.72
PVR	-2.32	IGF2R	-2.41	DNM3OS	-2.50	DLG2	-2.74
HOXB5	-2.32	GCLM	-2.41	TCN2	-2.51	THSD1	-2.74
HLA-B	-2.32	AK4	-2.41	AF038185	-2.52	AKNA	-2.74
BMP7	-2.32	CISH	-2.42	EYA4	-2.52	AK092921	-2.75
KIAA0930	-2.32	CHD7	-2.42	FAT1	-2.52	A_23_P314024	-2.76
PGM3	-2.33	FAM3C	-2.42	STXBP1	-2.53	TSC22D3	-2.76
PPP1R15A	-2.33	SPRY4	-2.42	C6orf168	-2.54	FDFT1	-2.76
ASPH	-2.33	RRAGB	-2.43	GLA	-2.54	SRXN1	-2.78
CCL27	-2.33	GABARAPL3	-2.43	HES1	-2.55	AKAP12	-2.79
B4GALT5	-2.33	TMEM87B	-2.43	S81524	-2.56	SLC17A5	-2.79
GTPBP4	-2.33	UNC13A	-2.43	COL3A1	-2.56	ENOX1	-2.79
NEU1	-2.33	CYP51A1	-2.44	TAC1	-2.57	PIK3C3	-2.79
CDK20	-2.34	SIRPA	-2.44	SQLE	-2.57	IGF2R	-2.80
ANXA5	-2.34	LONRF1	-2.44	NDUFAF4	-2.58	SREBF2	-2.80
EID3	-2.35	NHSL1	-2.45	B4GALT5	-2.58	ZNF263	-2.80
SLC30A7	-2.35	SEC63	-2.45	NAB2	-2.58	SNX9	-2.80
KPNA5	-2.35	DUSP8	-2.45	TMEM41B	-2.58	HLA-A	-2.83
VMP1	-2.36	HTR7	-2.45	NP113399	-2.59	THC2698892	-2.84
A_24_P33055	-2.37	IDUA	-2.45	INPP5K	-2.59	AY227436	-2.85
ATP1B1	-2.37	ITPRIPL2	-2.45	LOC643837	-2.59	GABARAPL1	-2.85
MYOF	-2.37	INPP5K	-2.46	RNASET2	-2.59	REEP3	-2.87
SSH3	-2.37	ATF3	-2.46	GPR56	-2.60	JUN	-2.88
OPTN	-2.37	SEZ6L2	-2.46	CHD7	-2.61	ARNT2	-2.88
BC013295	-2.37	CBX6	-2.47	SLC7A11	-2.61	NFYA	-2.90

Appendix I Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
UNC5B	-2.90	CD164	-3.20	HRC	-3.80	ALDH1A1	-4.64
MICA	-2.91	ADAM23	-3.20	EPAS1	-3.80	HLA-DMA	-4.75
A_32_P173922	-2.92	MMAB	-3.22	MICB	-3.81	SCD	-4.76
MAFG	-2.93	DLG2	-3.23	TMEM181	-3.83	ZDHHC14	-4.85
DACT1	-2.97	LIPA	-3.28	MMP10	-3.83	TRIB3	-4.88
STARD4	-2.97	EPHA3	-3.30	HOXB6	-3.83	COL5A1	-5.02
PDCD2	-2.98	HIST2H2AA4	-3.31	LRP8	-3.85	BIRC3	-5.04
PNPLA3	-2.98	GADD45A	-3.32	CCPG1	-3.85	ATF5	-5.06
MXD1	-2.99	F10	-3.33	TRPM3	-3.86	DB534761	-5.07
ZNF642	-2.99	TDRD3	-3.33	MIR137HG	-3.86	CAMK2N1	-5.13
MTRF1L	-3.00	CELF6	-3.38	DHCR24	-3.87	DMD	-5.16
OSTM1	-3.01	CACNA1B	-3.41	SCD	-3.87	TRIB3	-5.18
WIPI1	-3.01	PRAMEF8	-3.42	LOC100131053	-3.87	HMGCR	-5.24
GABARAPL1	-3.01	SH3GL3	-3.42	SCD	-3.87	PLK2	-5.28
TNFRSF12A	-3.01	ELL2	-3.44	DHCR24	-3.95	FGG	-5.30
ZNF469	-3.02	HOXB13	-3.45	CEACAM19	-3.96	RELB	-5.34
ITGAV	-3.02	TMEM41B	-3.45	THC2675966	-3.96	ARMC9	-5.44
MICB	-3.03	EPHA3	-3.45	HMGCS1	-3.98	INSIG1	-5.51
SARS	-3.03	LHX2	-3.47	C14orf37	-4.00	SPP1	-5.61
HLA-H	-3.03	ACAT2	-3.51	THC2675062	-4.01	EGR1	-5.80
LOC286382	-3.03	A_32_P145159	-3.53	ARMC9	-4.02	ACSS1	-5.94
ASPHD2	-3.04	SHC1	-3.54	NEAT1	-4.13	MMP3	-6.17
CD24	-3.05	HIST2H2AA4	-3.55	SCN7A	-4.17	SC5DL	-6.21
JHDM1D	-3.05	DDIT3	-3.56	RIPPLY2	-4.20	LIF	-6.22
FXYD1	-3.05	RAB7B	-3.57	ARHGEF2	-4.20	MSMO1	-6.22
LRP8	-3.08	MAFF	-3.58	SCN7A	-4.20	ARMC9	-6.28
S100A1	-3.12	LDLR	-3.58	THC2484716	-4.21	HTRA3	-6.28
A_24_P853366	-3.12	MGC23284	-3.59	SC5DL	-4.23	HMGCS1	-6.98
GPR137B	-3.12	LZTS1	-3.60	F2R	-4.23	KBTBD11	-7.17
HIST1H2BK	-3.12	LDLR	-3.60	A_23_P421323	-4.23	FGB	-7.31
RNF217	-3.13	A_23_P147404	-3.62	EFCAB1	-4.27	BC005081	-7.42
AKAP12	-3.16	DHCR7	-3.64	FOXD2	-4.28	HOXB9	-7.55
SGCA	-3.16	FNDC1	-3.67	HLA-DPA1	-4.38	A_23_P73096	-7.55
CHADL	-3.16	SOSTDC1	-3.70	IGF2	-4.39	ST3GAL1	-7.87
BACE2	-3.16	REEP3	-3.73	SC5DL	-4.45	ANK3	-8.15
MTRF1L	-3.17	CCPG1	-3.74	FAM129A	-4.48	LMF1	-8.65
CCPG1	-3.18	ACAT2	-3.74	THC2644672	-4.52	COL5A1	-8.67
ITGAV	-3.19	IDI1	-3.78	FAM129A	-4.57	ODZ2	-8.72
GDF15	-3.20	SQSTM1	-3.80	BEGAIN	-4.58	HMOX1	-8.75

Appendix I Gene Expression Changes in $A2780_{CBN-DXL}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
EFNA5	-9.32	ANK3	-9.87	CFH	-13.99	GPR84	-18.19
CFH	-9.44	A2M	-10.39	CR749547	-14.93	PTPN3	-18.79
LIPG	-9.55	ANK3	-11.21	A_23_P123234	-15.03	LIPG	-19.71
QKI	-9.77	CFHR3	-11.61	HSPA12A	-15.87	LONRF2	-22.32
ANK3	-9.80	AKR1C1	-11.76	KLHL29	-16.77		
TSHZ3	-9.82	CFH	-13.91	PRDM13	-17.56		

Appendix II Gene Expression Changes in $A2780_{CBN-CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
HSD17B12	309.26	PAIP2B	8.62	F11R	5.29	DNAJC22	4.32
MUC15	77.14			CU679648	5.16	MUC4	4.32
FAM9C	66.31	BMF	8.62	PPP1R1C	5.14	THC2493376	4.26
GSTT2	44.61	FAM9C	8.50	PDGFRA	5.12	AF086154	4.25
ATP1A2	42.91	ENST00000456585	8.39	PAX9	5.12	HSPB2	4.24
GSTT2	36.53	KLHDC9	8.39	HSBP1L1	5.07	AF034187	4.24
FAM9C	31.80	IRX5	7.84	FAM122C	5.03	AK054718	4.23
MGP	27.47	MXRA8	7.74	IRX3	5.02	AKR1C3	4.22
APOL6	23.17	MEOX1	7.32	ASRGL1	4.99	VAMP8	4.20
NFE2	23.12	IL22RA1	7.23	ANXA9	4.96	C19orf21	4.18
BST2	22.16	HOGA1	7.19	USP18	4.93	HMMR	4.18
SERPINB1	20.56	DKFZP564C152	6.99	RBPMS	4.91	LOXL1	4.13
DLGAP1	20.09	RBM24	6.99	GLYATL1	4.87	PRIM2	4.13
L1TD1	18.18	TES	6.80	C18orf34	4.87	MTL5	4.12
FOXA1	17.50	LRMP	6.80	TM4SF1	4.85	PRPH	4.08
AK021866	17.36	THC2658802	6.75	KCTD19	4.85	NTF4	4.03
THC2524341	17.12	ENST00000428928	6.69	CLDN1	4.85	MMP12	4.03
PAX9	16.02	CNTNAP2	6.62	SAA1	4.82	ASRGL1	4.02
FGF18	15.73	FES	6.62	HSBP1L1	4.81	APOBEC3C	4.02
TM4SF4	15.63	LTK	6.59	RASSF4	4.81	ENST00000531488	4.01
RBM24	15.12	THC2654127	6.45	CGNL1	4.80	USP18	3.97
MMP3	14.67	FAM84B	6.37	KRT222	4.77	SLC12A6	3.97
KLHL14	14.65	SLC39A8	6.32	CORO2A	4.76	WFDC5	3.96
BHLHE41	14.60	CSGALNACT1	6.26	CORO2A	4.70	LOC644662	3.95
CCRL2	13.74	DUSP27	6.19	THC2694800	4.69	THC2575678	3.95
LAYN	13.13	THC2698970	6.18	PLEKHA2	4.62	A_32_P112546	3.94
SPON2	13.10	CACNG6	6.09	PERP	4.59	LACC1	3.93
BX107298	13.01	ADM	5.94	ZFP42	4.58	ERBB4	3.91
HSD17B12	12.75	OTOL1	5.75	C15orf33	4.54	SLC16A4	3.87
PCDH7	12.55	ASB9	5.73	LOC100505683	4.54	C18orf56	3.86
DCLK1	12.46	MPZL3	5.65	GPR162	4.53	TAS1R1	3.85
EPN3	10.68	MXRA8	5.64	ERV9-1	4.51	MID1	3.83
PLAC8	10.58	SLC15A3	5.56	CSPG4	4.45	AKR1C1	3.82
EFEMP2	10.18	RAB3D	5.54	SERPINB9	4.44	MANSC1	3.80
SERPINB9	9.62	HOTAIR	5.52	DLX4	4.40	DDB2	3.80
HSPA1A	9.38	FAM92B	5.47	H19	4.39	ENPP6	3.79
PLAC8	9.25	C16orf86	5.47	A_32_P115707	4.39	APOBEC3F	3.79
GSG1	9.15	OASL	5.42	IGFLR1	4.39	CR598370	3.78
PLAU	8.87	PAIP2B	5.33	ENST00000502419	4.37	LOC439911	3.76
FOXA1	8.71	PACSIN1	5.32	COL16A1	4.32	DLK1	3.75
FGF18	8.63			THC2642537	4.32	C1RL	3.75

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ALDH6A1	3.73	BET3L	3.39	TOM1L2	3.17	SLC7A7	2.97
TNFRSF14	3.73	TBX15	3.39	BC037328	3.17	MAP2K6	2.97
RAB3B	3.73	CGN	3.39	GK	3.15	APOLD1	2.96
CA14	3.72	DUSP19	3.38	AL355688	3.14	MT1L	2.95
FAM183B	3.67	GRRP1	3.38	COL9A3	3.14	THC2757602	2.95
AKR1C1	3.67	GK	3.37	ACVRL1	3.13	HIST1H4B	2.95
MYCL1	3.66	A_24_P928830	3.36	PRPH2	3.13	CRIP2	2.94
ATP8B3	3.64	HNRNPM	3.36	THC2731337	3.13	RFC3	2.94
GNB5	3.64	KCNRG	3.36	C8orf51	3.10	LCP1	2.93
ATP8B3	3.63	CP	3.36	UCP2	3.10	A_32_P65157	2.93
ACTL8	3.63	FBXL5	3.35	HERC6	3.08	B3GNT8	2.92
STAU2	3.62	EFHC2	3.34	LRRC17	3.08	A_23_P66347	2.92
SORT1	3.60	ELF4	3.33	PTPN6	3.07	THC2652887	2.92
FGF21	3.60	A_32_P80523	3.32	COLEC11	3.06	A_24_P341546	2.91
DFNB31	3.58	LOC100506310	3.31	MT1X	3.06	SERP1	2.91
AF339799	3.58	RAB3D	3.31	AK129542	3.05	FUT1	2.91
CYP26A1	3.58	ENST00000421735	3.30	AF086044	3.05	DLGAP5	2.91
ASRGL1	3.56	C6orf52	3.30	SATB2	3.05	THC2652707	2.90
ARHGAP4	3.53	HIST1H1A	3.30	SPC25	3.04	NOTCH4	2.89
LOC100289361	3.53	MT2A	3.30	ENST00000443631	3.04	TMEM106C	2.88
BM552308	3.53	LOC100505679	3.29	BC030106	3.04	PDE11A	2.87
ENST00000452336	3.52	EOMES	3.29	NUDT7	3.03	PUS7L	2.87
CASP10	3.52	THC2638666	3.28	LOC729887	3.02	FAM47E	2.87
TMEM88	3.52	LOC644192	3.27	GLRX	3.02	PBK	2.85
ABCA1	3.51	RAB3B	3.26	AK125351	3.02	PTTG1	2.84
MIR210HG	3.48	PTH2	3.26	THC2671532	3.02	SAA2	2.84
THC2582300	3.48	LXN	3.25	A_24_P418216	3.02	KBTBD3	2.82
JUP	3.47	PTTG2	3.24	TRIM6	3.02	CYB5R2	2.82
CASP10	3.47	SDC2	3.23	THC2650514	3.02	HIST1H4L	2.82
KIAA0101	3.47	RASSF4	3.23	MBD2	3.01	PTTG3P	2.81
MT2A	3.46	ST7-AS1	3.23	THC2538534	3.01	PYGM	2.81
ASXL3	3.46	RAB3B	3.23	BG612665	3.00	TBXA2R	2.81
ARG2	3.45	BUB1	3.20	CCDC24	3.00	MID1	2.81
MAP2K6	3.45	AS3MT	3.19	THC2685994	3.00	FBXO15	2.81
MT2A	3.45	ENST00000539135	3.19	THC2655094	2.99	STK33	2.81
ARHGDIB	3.44	CCNB2	3.18	MT1E	2.99	ENST00000507916	2.81
S100A16	3.43	LDB3	3.18	WDR78	2.99	SIPA1	2.80
SPC24	3.43	HEYL	3.17	VASN	2.99	ENST00000452565	2.80
LOC400604	3.43	C9orf100	3.17	TMEM107	2.98	FOLR1	2.79
PLIN5	3.42	LOC100506059	3.17	LDHD	2.98	KRTAP19-1	2.79
ZDHHC12	3.41			CCNB3	2.98		

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
FAM183A	2.79	C2orf89	2.65	ENST00000551187	2.53	HMGB2	2.45
MT1X	2.78	CRYAB	2.64	SCD5	2.53	IGFBP2	2.45
PRKCH	2.78	LOC440434	2.64	NCAPG2	2.53	GPR4	2.45
BU602485	2.78	AF086547	2.64	MT1G	2.53	DHX58	2.45
SNX5	2.77	THC2499508	2.64	LHX2	2.52	CCDC109B	2.45
ENST00000432751	2.77	KIF20A	2.63	THC2646608	2.52	AMPD3	2.44
C1QTNF6	2.77	SLC44A1	2.63	FOXD1	2.52	TMEM107	2.44
FOXN4	2.76	HIST1H4C	2.62	DERA	2.52	GCAT	2.44
NDC80	2.76	U88048	2.62	APAF1	2.52	BTN2A2	2.44
GAL3ST1	2.76	USP41	2.60	AGBL2	2.51	LOC644656	2.44
ENST00000537149	2.76	TLX3	2.60	RDM1	2.51	THC2697412	2.44
PRSS16	2.76	BM458245	2.59	ENST00000429480	2.51	A_24_P49657	2.44
TRIM6	2.75	PNKD	2.59	CD511705	2.51	NEURL1B	2.43
CD34	2.73	ENPP6	2.59	RRM2	2.50	A_24_P560431	2.43
SHMT1	2.73	TXNIP	2.59	DEPDC1	2.50	ENST00000356370	2.43
TRIM34	2.73	SAMD14	2.59	HIST1H1D	2.50	OCA2	2.42
BC032755	2.72	CEP44	2.59	LOC100507568	2.50	H2AFJ	2.42
LOC389493	2.72	DMBX1	2.58	SLC44A1	2.49	OIP5	2.42
A_23_P72014	2.72	CRIP1	2.58	HIST1H2BD	2.49	SYT5	2.42
CCDC80	2.71	CDCA2	2.58	TK1	2.49	BQ933774	2.42
LOC100129794	2.71	C6orf226	2.58	RAB26	2.49	CLGN	2.42
RFTN2	2.70	CETN4P	2.58	TNNC1	2.49	PIH1D2	2.41
TES	2.70	A_24_P84711	2.58	CNTNAP2	2.49	TMEM237	2.41
ENST00000420759	2.70	HIST1H4D	2.57	PRIM1	2.49	DLG3	2.41
FLJ37453	2.70	IFI30	2.57	LOC100128822	2.48	CASC5	2.41
THC2689749	2.69	FRY	2.57	FGD6	2.48	BCAS4	2.41
BET3L	2.68	CABP1	2.57	PPPDE1	2.48	NGEF	2.41
LOC100507303	2.68	SAMD14	2.57	DZIP3	2.48	LOH12CR2	2.40
TNNT2	2.68	IKZF2	2.56	NT5DC1	2.47	THC2753400	2.40
ENST00000394813	2.68	THC2507877	2.56	CU686711	2.47	THC2651534	2.40
C21orf119	2.68	BTN2A2	2.55	DDT	2.47	TNNI3	2.40
BDH2	2.67	NDC80	2.55	KIF11	2.47	ABLIM1	2.40
HOXC11	2.67	LOC100128511	2.55	ATCAY	2.47	U2AF1	2.40
AKAP5	2.67	NT5DC1	2.55	DHTKD1	2.47	C16orf55	2.40
MT1H	2.67	LOC100652730	2.55	MFAP4	2.47	SOD2	2.40
THC2537856	2.66	EFCAB11	2.54	PRR11	2.47	LYL1	2.39
TRIM15	2.65	BQ881683	2.53	GPSM2	2.46	PELI1	2.39
AB593167	2.65	A_24_P902195	2.53	CSTF3	2.46	CFL2	2.39
PTPRF	2.65	PHIP	2.53	SNHG13	2.46	SPOCD1	2.39
		C21orf58	2.53	THC2541678	2.46	TCEAL3	2.38
		GPER				ATP2B4	2.38

Appendix II Gene Expression Changes in $A2780_{CBN-CC}$ vs. $A2780_{CBN}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ASF1B	2.38	ENST00000430027	2.31	RAD54B	2.24	BAIAP2L2	2.19
TMEM187	2.38	BIRC5	2.30	IFI27	2.24	CDK19	2.19
IFITM1	2.38	RFX5	2.30	CEP70	2.24	STMN1	2.19
NRG1	2.37	SCRG1	2.30	LOC81691	2.24	TMED4	2.19
GNG7	2.37	SLC25A21	2.30	PPFIA4	2.24	KANK2	2.19
CCDC24	2.37	HIST2H2AC	2.29	THC2707492	2.24	TTK	2.18
GKAP1	2.37	ENST00000557691	2.29	THC2603239	2.23	FLJ35024	2.18
CCDC116	2.37	PSRC1	2.29	AES	2.23	RAD51C	2.18
LOC100506190	2.37	ERMP1	2.29	TMEM237	2.23	FAM113B	2.18
AP1M2	2.37	DHRS2	2.29	DNAJC12	2.23	DEPDC1	2.18
PACSIN1	2.37	CABYR	2.29	ANKRD45	2.23	BC029907	2.17
PPP1R12B	2.36	BC038747	2.28	THC2677286	2.23	KIAA1522	2.17
GMIP	2.36	ATOH7	2.28	AGT	2.23	DEPDC4	2.17
A_32_P209163	2.36	KIAA0586	2.28	P2RX5	2.23	THC2756581	2.17
CFD	2.36	BC012528	2.28	TET1	2.23	COLEC11	2.17
ENST00000555442	2.36	NUDT6	2.28	HSDL2	2.23	EXTL1	2.17
ATP2A3	2.35	MEGF6	2.28	A_24_P938006	2.22	SPAG5	2.17
A_32_P75141	2.35	TMEM37	2.28	BTBD8	2.22	AK124097	2.17
DHFR	2.35	THC2677011	2.27	TCF4	2.22	A_32_P99804	2.17
FLOT2	2.35	LOC100130890	2.27	FBXO3	2.22	CCNG2	2.16
LOC730102	2.35	RGS3	2.27	ENST00000424852	2.22	LOC100507475	2.16
S100A4	2.35	DZIP3	2.27	A_32_P57002	2.21	HIP1	2.16
CPPED1	2.35	LDHC	2.27	CARD8	2.21	ENST00000419207	2.16
HIST1H1B	2.35	CCNA2	2.27	NYNRIN	2.21	MFNG	2.16
TCEAL5	2.34	CDC45	2.26	DNAJC15	2.21	A_23_P392897	2.16
NEIL3	2.33	CDC25C	2.26	MYLK	2.21	UBR1	2.16
MCF2L	2.33	STRADB	2.26	LOC100506190	2.21	STAC2	2.16
CHCHD10	2.33	ABAT	2.26	LOC730101	2.21	ARAP1	2.15
TOM1L2	2.33	ENO3	2.26	TNS1	2.21	BRIP1	2.15
MGST2	2.33	ABCC6	2.26	LOC100506236	2.21	DNMT3B	2.15
MELK	2.33	OLFML2A	2.26	FZR1	2.21	AK1	2.14
BCKDHB	2.33	ZC3H6	2.26	LOC401052	2.21	FAM82A1	2.14
TMEM35	2.33	WWOX	2.26	IQCD	2.20	RASIP1	2.14
TGFB3	2.32	KIAA0586	2.25	BDH2	2.20	LOC100505616	2.14
AK023629	2.32	E2F8	2.25	CENPF	2.20	NEK2	2.14
CARHSP1	2.32	ADPRHL1	2.25	CIT	2.20	HIST1H4K	2.14
PDCD4	2.31	RGS9BP	2.25	NMU	2.19	CDCA3	2.14
CCR1	2.31	ALDH4A1	2.24	VSIG10	2.19	TCEAL6	2.14
PRIM2	2.31	HIST1H4J	2.24	BC018626	2.19	TGM2	2.14
C6orf165	2.31	FANCI	2.24	CBX7	2.19	A_32_P46351	2.13
CSRP2	2.31			TRERF1	2.19	LOC100506268	2.13

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
CUL5	2.13	GYS1	2.06	ENST00000456688	2.01	PP7080	-2.01
ENST00000449075	2.13	KIRREL2	2.06	DHFR	2.01	LINC00265	-2.01
CENPE	2.13	ITGB3BP	2.06	MXD3	2.01	FAM21C	-2.01
LOC645676	2.12	PIN4	2.06	WDHD1	2.01	PLEKHF1	-2.01
DHRS3	2.12	CRYBB2	2.06	CEP70	2.00	TMEM22	-2.01
NCAPG	2.12	SYTL4	2.06	C6orf211	2.00	FBRSL1	-2.01
ESCO2	2.12	AK057740	2.06	TPM1	2.00	PCYT1A	-2.01
DOCK3	2.12	ITGA6	2.05	AURKB	2.00	XPR1	-2.01
TMEM14A	2.11	FAM82A1	2.05	A_24_P332953	2.00	A_24_P290046	-2.01
CBX7	2.11	DHRS11	2.05	LRPAP1	-2.00	BIRC2	-2.01
JMJD7	2.11	ASPM	2.05	MMAB	-2.00	PITPNA	-2.01
CENPI	2.11	A_24_P323682	2.05	TMEM9B	-2.00	AF321778	-2.01
THC2596018	2.11	ABHD8	2.05	ANKRD11	-2.00	A_32_P177595	-2.01
INPP5D	2.11	NUSAP1	2.05	A_23_P136296	-2.00	IGDCC3	-2.01
PVRL2	2.11	A_24_P126741	2.05	E2F5	-2.00	VSTM4	-2.01
AV707615	2.10	LOC100506659	2.04	A_32_P331700	-2.00	PCYT1A	-2.01
A_24_P221285	2.10	POLR3GL	2.04	B3GALNT2	-2.00	AP3S2	-2.01
SLC38A4	2.10	AK123584	2.04	KIAA1539	-2.00	DLG4	-2.01
IFI27	2.10	MTMR9LP	2.04	AK4	-2.00	SNX29	-2.01
H1FX	2.10	DHFR	2.04	PTP4A2	-2.00	MPP3	-2.01
NDRG4	2.09	FDXR	2.04	MBNL3	-2.00	PRRC2B	-2.01
CCNB1	2.09	ANLN	2.04	TNPO2	-2.00	HMBOX1	-2.02
MT1B	2.09	SGCA	2.04	A_32_P327750	-2.00	ENST00000416851	-2.02
AKR1B1	2.09	BAD	2.04	THC2748290	-2.00	AF187554	-2.02
CDKN3	2.09	PRAME	2.04	FOXE3	-2.00	ZFAND3	-2.02
AA019203	2.09	ANK1	2.04	C22orf25	-2.00	ABTB2	-2.02
SLC25A10	2.08	HIST1H2AL	2.04	CHRDL1	-2.00	TMEM33	-2.02
HIST1H4E	2.08	A_32_P219377	2.04	PTCH1	-2.00	MKRN1	-2.02
DIDO1	2.08	AK054902	2.03	LOC643669	-2.00	C7orf40	-2.02
LOC100506922	2.08	TNFAIP8	2.03	TCAP	-2.01	BC042589	-2.02
PHYHD1	2.08	AATK	2.03	HYOU1	-2.01	A_24_P332780	-2.02
RRM1	2.08	PIP5KL1	2.03	NOP56	-2.01	GLT25D2	-2.02
SGOL1	2.08	GPR19	2.03	PGS1	-2.01	C8orf31	-2.02
SLC44A1	2.08	C16orf74	2.03	A_32_P22005	-2.01	P2RY1	-2.02
NUDT16L1	2.08	ECT2	2.02	MINA	-2.01	SLC38A6	-2.02
KIAA0182	2.08	LRRN3	2.02	C8orf42	-2.01	AK098134	-2.02
PI4K2B	2.07	GCHFR	2.02	PTP4A2	-2.01	RAB3IL1	-2.02
SGOL2	2.07	RASSF7	2.02	ZMYND19	-2.01	CEBPE	-2.02
HPS3	2.07	THC2657737	2.02	ANKRD28	-2.01	ZNF274	-2.02
CDC20	2.07	ATAD2	2.01	WWC1	-2.01	EIF2AK3	-2.02
KIF1B	2.06	THC2559752	2.01	A_24_P196134	-2.01	RAPGEF1	-2.02

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
MYBBP1A	-2.02	PSPH	-2.03	THBS1	-2.04	SOCS7	-2.06
A_24_P126731	-2.02	RNF157	-2.03	A_32_P30898	-2.04	ING5	-2.06
FAM134A	-2.02	ARHGAP17	-2.03	EZH1	-2.04	PAFAH2	-2.06
HEG1	-2.02	FAM198B	-2.03	THC2693398	-2.05	KAT6B	-2.06
HGS	-2.02	LOC84856	-2.03	BRWD1	-2.05	FEZ1	-2.06
GRINA	-2.02	ACTG1	-2.03	CD276	-2.05	ZNF706	-2.06
ADAM8	-2.02	ZNF259	-2.03	MICAL2	-2.05	PACRGL	-2.06
GTF2IRD2B	-2.02	CHGA	-2.03	E2F4	-2.05	METRNL	-2.06
A_24_P752208	-2.02	KIF7	-2.03	MARS2	-2.05	ANKLE1	-2.06
SHROOM1	-2.02	THC2524424	-2.03	PSMD11	-2.05	GPR125	-2.06
ZNF532	-2.02	CT47B1	-2.03	MAGI2	-2.05	A_24_P812172	-2.06
WASF3	-2.02	FTH1	-2.03	KLHL5	-2.05	RRP15	-2.06
LRRC8B	-2.03	CLCN3	-2.03	RAB24	-2.05	ELOVL6	-2.06
HRASLS5	-2.03	PLEKHF1	-2.04	PARP4	-2.05	MALT1	-2.06
KIAA0754	-2.03	C19orf43	-2.04	FAM92A1	-2.05	ARPC4-TTLL3	-2.06
SLC2A3	-2.03	THC2717825	-2.04	CLNS1A	-2.05	CA5B	-2.06
ZNF568	-2.03	RIOK3	-2.04	PDCD6IP	-2.05	TOR3A	-2.06
TOB2P1	-2.03	FLJ43663	-2.04	HDAC10	-2.05	JAM2	-2.07
FGR	-2.03	NPDC1	-2.04	LOC595101	-2.05	DNHD1	-2.07
TMEM18	-2.03	IMPAD1	-2.04	A_24_P912626	-2.05	RHOQ	-2.07
KIRREL	-2.03	HMGN1	-2.04	A_24_P307466	-2.05	B4GALT5	-2.07
PEA15	-2.03	CHMP4B	-2.04	RBMS3	-2.05	ACSS2	-2.07
CBX6	-2.03	A_32_P62137	-2.04	PXN	-2.05	ZNF174	-2.07
CSRNP2	-2.03	C8orf55	-2.04	OSBPL6	-2.05	ZFAND5	-2.07
C20orf194	-2.03	TMEM150A	-2.04	A_24_P127701	-2.05	C19orf28	-2.07
A_32_P96752	-2.03	ZCCHC18	-2.04	VCP	-2.05	LARP6	-2.07
CYP20A1	-2.03	A_32_P103474	-2.04	MLXIP	-2.05	LOC338620	-2.07
KLHDC5	-2.03	A_24_P41890	-2.04	MFGE8	-2.05	GAS6	-2.07
MKNK2	-2.03	PSAP	-2.04	MUC6	-2.05	SBNO1	-2.07
A_32_P214781	-2.03	BOD1	-2.04	PNMA3	-2.05	UCHL1	-2.07
PLEKHA4	-2.03	CCDC126	-2.04	CAPN12	-2.05	PRKCA	-2.07
LOC100506528	-2.03	HOPX	-2.04	TMEM22	-2.05	DKFZP586I1420	-2.07
OR1F2P	-2.03	GPD1	-2.04	IGLL1	-2.05	ZNF473	-2.07
RUNDC2C	-2.03	A_24_P290114	-2.04	KAT6B	-2.05	RHOQ	-2.07
NDUFC2	-2.03	ZFYVE9	-2.04	CLK2	-2.05	C2orf27A	-2.07
ZNF37BP	-2.03	A_24_P229726	-2.04	CHRNA10	-2.05	PPP2R2D	-2.07
BX102988	-2.03	TLE1	-2.04	ABCC8	-2.06	A_24_P101771	-2.07
CNN1	-2.03	SERBP1	-2.04	CCDC40	-2.06	ENST00000553155	-2.07
CYP4X1	-2.03	ZNF234	-2.04	C15orf37	-2.06	RET	-2.07
LAT	-2.03	ANKRD53	-2.04	SRRT	-2.06	AX229882	-2.07
DHX32	-2.03	MON1B	-2.04	BU903025	-2.06	A_24_P290068	-2.07

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
PTPRN	-2.07	ADO	-2.09	THC2744561	-2.10	ENDOD1	-2.11
TCP10	-2.07	RIOK1	-2.09	AK026869	-2.10	C16orf52	-2.11
ARID1A	-2.07	MPP3	-2.09	NSFL1C	-2.10	VPS13B	-2.11
C2CD2	-2.07	PI15	-2.09	A_24_P170309	-2.10	OLFML3	-2.11
FAM86C1	-2.07	A_32_P65934	-2.09	A_24_P681266	-2.10	A_24_P366465	-2.11
JMJD1C	-2.07	YTHDC1	-2.09	RUNX2	-2.10	IL17RA	-2.11
NBPF10	-2.07	TRIML2	-2.09	MAP3K2	-2.10	MGC23284	-2.11
BG118529	-2.07	A_32_P83305	-2.09	ZNF337	-2.10	MAVS	-2.12
RGS11	-2.07	CLK2	-2.09	ZFYVE28	-2.10	EXOSC6	-2.12
THC2635591	-2.07	CASD1	-2.09	MLLT6	-2.10	PCYT1B	-2.12
NBPF10	-2.07	EME2	-2.09	PTPRH	-2.10	LOC100506710	-2.12
SLC12A7	-2.08	CERS5	-2.09	PVR	-2.10	MUC3	-2.12
PRKG1	-2.08	A_24_P247175	-2.09	LOC729234	-2.10	UBE2G2	-2.12
NUMBL	-2.08	HOXC10	-2.09	COL20A1	-2.10	ZNF697	-2.12
F2R	-2.08	TMEM33	-2.09	AK000420	-2.10	ACSL4	-2.12
THC2686940	-2.08	CD46	-2.09	TESK1	-2.10	A_32_P128773	-2.12
CEBPD	-2.08	ASMTL	-2.09	HS6ST2	-2.10	TRIO	-2.12
AHI1	-2.08	A_32_P194182	-2.09	TYRP1	-2.10	ACHE	-2.12
PDCD6IP	-2.08	PP14571	-2.09	FAM21A	-2.10	POLR2A	-2.12
A_24_P204574	-2.08	KCTD1	-2.09	A_24_P499282	-2.10	ADCY9	-2.12
TUSC1	-2.08	PCSK6	-2.09	ZNF114	-2.10	MDN1	-2.12
NBPF9	-2.08	PTPRD	-2.09	SLC25A37	-2.10	COL4A3BP	-2.12
X03757	-2.08	EMP1	-2.09	A_32_P149625	-2.10	SETD5	-2.12
BTNL2	-2.08	FAM120A	-2.09	KLHDC5	-2.10	MMP23B	-2.12
MKNK2	-2.08	A_24_P350136	-2.09	ZNF521	-2.11	MED10	-2.12
C18orf49	-2.08	POTED	-2.09	AI140519	-2.11	LOC100125556	-2.12
ARRDC2	-2.08	CCDC93	-2.09	CEP104	-2.11	BC016384	-2.12
PLCL2	-2.08	CYCS	-2.09	LCOR	-2.11	RAB22A	-2.12
GALNT11	-2.08	NTN1	-2.09	SYVN1	-2.11	SLC3A2	-2.12
MVK	-2.08	MAFIP	-2.09	RGR	-2.11	A_32_P174374	-2.12
ZNF140	-2.08	POSTN	-2.10	TNFAIP3	-2.11	AF086528	-2.12
ATRN	-2.08	CLASRP	-2.10	MYOF	-2.11	ENST00000553929	-2.13
SHANK3	-2.08	BEST1	-2.10	MAX	-2.11	ZNF689	-2.13
MFSD2A	-2.08	PPIE	-2.10	MS4A1	-2.11	UGGT2	-2.13
TH1L	-2.08	SOX4	-2.10	FOXO3	-2.11	CLCN7	-2.13
AK021777	-2.08	SEMA4C	-2.10	CD86	-2.11	EDEM3	-2.13
GDF3	-2.09	TOP1MT	-2.10	RASAL3	-2.11	TUSC1	-2.13
VCL	-2.09	A_24_P127661	-2.10	MYOF	-2.11	ITPRIPL2	-2.13
VGF	-2.09	THC2712190	-2.10	PARP4	-2.11	ZNF704	-2.13
APLP2	-2.09	RHOQ	-2.10	DIS3L2	-2.11	COL6A3	-2.13
AK026418	-2.09	TMEM151B	-2.10	AGAP8	-2.11	UBXN8	-2.13

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ENST00000378337	-2.13	CSRNP1	-2.14	FCN1	-2.16	HBEGF	-2.17
KLF13	-2.13	AF090927	-2.14	ITGB2	-2.16	GJA4	-2.17
SLC5A3	-2.13	ZNF551	-2.14	CCNY	-2.16	HIST1H1C	-2.17
AK022299	-2.13	ZNF136	-2.14	A_24_P375870	-2.16	ZNF529	-2.17
CHADL	-2.13	MED13L	-2.14	MFGE8	-2.16	A_24_P332721	-2.17
HOXC8	-2.13	GPR135	-2.14	A_32_P165993	-2.16	A_32_P9931	-2.17
THC2656826	-2.13	KIAA0368	-2.14	A_24_P16090	-2.16	ZNF202	-2.17
A_32_P73491	-2.13	SLC25A38	-2.14	PFKFB2	-2.16	KCNK6	-2.17
CLIP1	-2.13	A_24_P32715	-2.14	SNX29	-2.16	ARHGEF10	-2.17
CCDC142	-2.13	A_32_P23872	-2.14	THC2702563	-2.16	SLC35E1	-2.17
DNAJB2	-2.13	SGMS1	-2.15	ELMO3	-2.16	A_24_P650562	-2.17
NBPF3	-2.13	THC2706736	-2.15	ZNF343	-2.16	INO80D	-2.17
DNASE1L2	-2.13	IRF1	-2.15	CACNG5	-2.16	BEND3	-2.17
C5orf25	-2.13	EP300	-2.15	MYH9	-2.16	PPFIBP2	-2.17
C9orf21	-2.13	XR_017086	-2.15	FYN	-2.16	UPP1	-2.17
CCNY	-2.14	A_24_P263803	-2.15	THC2538610	-2.16	H2BFXP	-2.17
B3GNT9	-2.14	LOC100507460	-2.15	CLCF1	-2.16	TSNARE1	-2.17
GRIA4	-2.14	PHF11	-2.15	GOLGA3	-2.16	THC2510958	-2.17
A_23_P78975	-2.14	GOLGA8F	-2.15	POGLUT1	-2.16	LRRC8B	-2.17
THC2719547	-2.14	SPRY4	-2.15	RNFT1	-2.16	LOC100132790	-2.18
SLC7A3	-2.14	NBPF11	-2.15	A_32_P47616	-2.16	WDR19	-2.18
MINA	-2.14	THC2727164	-2.15	KANSL3	-2.16	MCL1	-2.18
CYB5R1	-2.14	MXD1	-2.15	RHO	-2.16	RRS1	-2.18
NOC2L	-2.14	TECPR2	-2.15	MAPK8IP3	-2.16	RBM19	-2.18
OVGP1	-2.14	A_32_P27558	-2.15	SACS	-2.16	FMNL2	-2.18
PPAPDC1B	-2.14	ACAP3	-2.15	A_24_P384469	-2.16	POM121	-2.18
R3HDM2	-2.14	NKX6-3	-2.15	PIGH	-2.16	FAM43B	-2.18
A_24_P914957	-2.14	N4BP3	-2.15	MAX	-2.16	UGGT2	-2.18
ENST00000491977	-2.14	THC2674068	-2.15	EPT1	-2.16	TTC39A	-2.18
SH3RF2	-2.14	WIPF3	-2.15	HOXC10	-2.16	RHPN1	-2.18
ZNF407	-2.14	AK025430	-2.15	PYGO1	-2.16	TRAF3	-2.18
CLDN8	-2.14	ABHD4	-2.15	MAP3K2	-2.17	ACTN2	-2.18
A_24_P212997	-2.14	SMOX	-2.15	A_24_P152345	-2.17	POU6F1	-2.18
MTRF1L	-2.14	ZNF26	-2.15	WDFY4	-2.17	PHTF1	-2.18
THC2593778	-2.14	ENST00000512848	-2.15	DNAJC5G	-2.17	A_24_P636974	-2.18
LIFR	-2.14	ESX1	-2.15	CDHR1	-2.17	ATP10A	-2.18
DPH2	-2.14	SRSF7	-2.16	UNC13A	-2.17	IRS2	-2.18
TMC8	-2.14	THC2640304	-2.16	ZSWIM6	-2.17	CLK2	-2.18
RNASET2	-2.14	HEXB	-2.16	VASH1	-2.17	SETX	-2.18
TSPAN9	-2.14	ZNF181	-2.16	UTP14A	-2.17	DFFB	-2.18
		NPEPL1	-2.16	A_24_P237896	-2.17	SARS	-2.18

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
HMX2	-2.19	FLVCR1	-2.20	DNAJC25	-2.22	DCAF4	-2.23
THC2766373	-2.19	CEACAM1	-2.20	BAG3	-2.22	A_24_P153342	-2.23
ZNF259P1	-2.19	OXCT2	-2.20	PVR	-2.22	SDK2	-2.23
SETD4	-2.19	PCMTD2	-2.20	CB162722	-2.22	BG571904	-2.23
BRWD1	-2.19	C20orf3	-2.20	AK090463	-2.22	ASAP1	-2.24
A_24_P496034	-2.19	POTEF	-2.20	KLK8	-2.22	TMEM198	-2.24
PPFIBP1	-2.19	PHC2	-2.20	MGAT4B	-2.22	ZNF704	-2.24
ACTR3B	-2.19	LOC96610	-2.20	THC2512545	-2.22	RNF185	-2.24
ACTB	-2.19	NFKB1	-2.20	NACC1	-2.22	EXT1	-2.24
LOC100132790	-2.19	DNM3OS	-2.20	BU929651	-2.22	A_32_P90615	-2.24
KIRREL	-2.19	SOCS1	-2.21	ANKRD11	-2.22	PODXL2	-2.24
CAMTA1	-2.19	SOCS6	-2.21	LRRN2	-2.22	IPO7	-2.24
BX440400	-2.19	ITFG2	-2.21	CHPF2	-2.22	GOLGA8A	-2.24
A_24_P577289	-2.19	ZNF2	-2.21	THC2541992	-2.22	BC004387	-2.24
ENST00000434871	-2.19	THC2746807	-2.21	LRP1	-2.22	ENPP7	-2.24
KLHL5	-2.19	PPARGC1B	-2.21	ZNF275	-2.23	A_24_P933940	-2.24
AK123264	-2.19	A_32_P107441	-2.21	ACACA	-2.23	FBLN7	-2.24
SAMD4B	-2.19	ENST00000440990	-2.21	A_32_P122951	-2.23	ZNF696	-2.24
CHD7	-2.19	DKFZp761E198	-2.21	ZNF473	-2.23	SLC29A2	-2.24
ENST00000377186	-2.19	TFE3	-2.21	METTL21A	-2.23	HIST1H2AD	-2.25
PI4KAP2	-2.19	AGPAT6	-2.21	SLC10A4	-2.23	RNF217	-2.25
PLXNA1	-2.19	THC2481891	-2.21	LOC401431	-2.23	GGA1	-2.25
ENST00000356801	-2.19	A_24_P144314	-2.21	LOC100506710	-2.23	EMP3	-2.25
THC2669419	-2.19	FOXO1	-2.21	A_24_P850172	-2.23	TRIM41	-2.25
AK094623	-2.20	BE184907	-2.21	ZFYVE28	-2.23	NDUFA4L2	-2.25
FOXO3	-2.20	SENP3	-2.21	ST3GAL1	-2.23	C9orf131	-2.25
ENST00000412513	-2.20	LOC100499177	-2.21	AF126109	-2.23	BC001335	-2.25
TNF	-2.20	CPS1-IT1	-2.21	A_24_P76288	-2.23	SLC12A7	-2.25
PLAUR	-2.20	CCDC88C	-2.21	ASCL1	-2.23	GTPBP4	-2.25
CSGALNACT2	-2.20	TBRG1	-2.22	LOC100131170	-2.23	A_23_P47220	-2.25
VDR	-2.20	TTC17	-2.22	MYBPC2	-2.23	GFPT1	-2.25
NRIP1	-2.20	CABP7	-2.22	OVOL2	-2.23	HSPA5	-2.25
PDIA2	-2.20	THC2664573	-2.22	SMCR5	-2.23	SLC37A3	-2.25
CYTH2	-2.20	NUAK2	-2.22	A_32_P204903	-2.23	UBQLN1	-2.25
OTUD7A	-2.20	ENST00000330588	-2.22	CRMP1	-2.23	SLC22A23	-2.25
ABAT	-2.20	LPP	-2.22	NPIPL2	-2.23	ZNF222	-2.25
HIPK2	-2.20	ZNF420	-2.22	ZCCHC2	-2.23	RAPGEF1	-2.25
RUFY3	-2.20	FTH1	-2.22	BMS1P1	-2.23	THC2719015	-2.26
SEC24D	-2.20	TXNDC11	-2.22	THC2619153	-2.23	BG534208	-2.26
		SLC38A7	-2.22	PRB4	-2.23	ARHGAP32	-2.26
				RNF144A	-2.23	AK023077	-2.26

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
MON1B	-2.26	SLC5A12	-2.28	66		GFOD1	-2.31
C11orf16	-2.26	PLD6	-2.28	TOLLIP	-2.30	MVK	-2.31
DNM3OS	-2.26	M15530	-2.28	DNAJB9	-2.30	ENST00000390539	-2.31
ENST00000399967	-2.26	AGAP7	-2.28	ITPKC	-2.30	TREML1	-2.32
A_32_P127812	-2.26	GOLGA8A	-2.28	PDGFD	-2.30	CAMKK1	-2.32
CCDC57	-2.26	ZNFX1	-2.28	NUP188	-2.30	ZNF669	-2.32
DGCR5	-2.26	LAMA2	-2.28	KLF2	-2.30	RAP1GAP2	-2.32
ATG7	-2.26	ASB13	-2.28	HSPA13	-2.30	A_24_P936393	-2.32
A_24_P712193	-2.26	KREMEN2	-2.28	KIAA1549	-2.30	C1orf216	-2.32
TMEM43	-2.26	NOL6	-2.28	DA093175	-2.30	THC2666547	-2.32
A_23_P125109	-2.26	ENST00000434399	-2.28	RPA4	-2.30	ZNF121	-2.32
PTPRJ	-2.26	SNAI2	-2.28	SEL1L	-2.30	ARIH2	-2.32
LOC653075	-2.27	HSPA5	-2.28	ZC3H7B	-2.30	A_32_P11701	-2.32
TIMP1	-2.27	DLST	-2.28	ZNF423	-2.30	A_24_P540555	-2.32
ACCN3	-2.27	STBD1	-2.28	GDF15	-2.30	A_24_P670342	-2.32
KCNN4	-2.27	UGCG	-2.28	ERO1LB	-2.30	JUND	-2.32
AV756170	-2.27	PCMTD2	-2.28	LRP8	-2.30	PPP2R2C	-2.32
HEMK1	-2.27	LINC00341	-2.28	ANKRD10	-2.30	VPS13A	-2.32
THC2694186	-2.27	RUNDC3A	-2.28	LAT	-2.30	NOB1	-2.32
THC2563568	-2.27	CPNE8	-2.29	A_24_P937424	-2.30	FAM90A7	-2.32
ZSCAN22	-2.27	EBF4	-2.29	CTTN	-2.30	AK024470	-2.32
A_32_P221552	-2.27	ENST00000427392	-2.29	SLC41A2	-2.30	LOC100507493	-2.32
ACTG1	-2.27	COL13A1	-2.29	BBC3	-2.30	A_24_P929985	-2.32
HM358951	-2.27	SEL1L	-2.29	PDXDC2P	-2.31	CACNA1B	-2.32
CCDC159	-2.27	ENST00000447898	-2.29	UBE2E1	-2.31	ENST00000468198	-2.33
TNPO2	-2.27	POM121L8P	-2.29	SLC25A37	-2.31	CLDN15	-2.33
TCF25	-2.27	WIPI1	-2.29	PDXDC2P	-2.31	AGAP8	-2.33
RNF217	-2.27	BBC3	-2.29	POTEE	-2.31	A_24_P76210	-2.33
AA151106	-2.27	POTEM	-2.29	THC2650120	-2.31	A_24_P493005	-2.33
FNTA	-2.27	ANKRD57	-2.29	TNXB	-2.31	TTC15	-2.33
HIPK2	-2.27	A_24_P927205	-2.29	JMJD5	-2.31	A_24_P383901	-2.33
NETO2	-2.27	UGCG	-2.29	COL12A1	-2.31	IFRD1	-2.33
NAT8L	-2.27	CHRD	-2.29	AK001057	-2.31	TRMT61A	-2.33
KLK5	-2.27	LOC100287482	-2.29	DPH2	-2.31	MOB3B	-2.33
KLHDC5	-2.27	FBLL1	-2.29	FXR2	-2.31	MVD	-2.33
SRSF1	-2.27	DDX10	-2.29	THC2651023	-2.31	A_32_P7193	-2.33
COL6A2	-2.27	SETBP1	-2.29	OR10J3	-2.31	C8orf59	-2.33
AL576526	-2.27	A_32_P139909	-2.29	THC2570021	-2.31	HUS1B	-2.33
ZRSR2	-2.27	MGAT5	-2.29	SLC6A19	-2.31	KLHL17	-2.33
FAM101A	-2.27	ENST00000453199	-2.29	NETO2	-2.31	NPPC	-2.33
AF086335	-2.28			MIR22HG	-2.31		

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
TXLNA	-2.33	HIST1H2BK	-2.36	RPS6KB1	-2.38	PRKAG2	-2.40
POTEKP	-2.33	CCDC144A	-2.36	PURB	-2.38	A_23_P206568	-2.40
KCNQ1	-2.34	CBFA2T3	-2.36	AK124426	-2.38	A_32_P49552	-2.40
WDR1	-2.34	CEBPA	-2.36	GHRLOS	-2.38	C6orf168	-2.40
LRRC41	-2.34	TRIM44	-2.36	AW972815	-2.38	SLC6A13	-2.40
MYO6	-2.34	MYOF	-2.36	FOSL2	-2.38	LOC399851	-2.40
CAPN1	-2.34	NFRKB	-2.36	RASL11B	-2.38	MZT2A	-2.40
DUSP16	-2.34	A_24_P306614	-2.36	SLC25A25	-2.38	KAT2B	-2.40
C21orf2	-2.34	HRC	-2.36	AF144054	-2.38	TMEM231	-2.40
FRMD4A	-2.34	RIOK1	-2.36	LOC100132593	-2.38	TRIO	-2.40
FAM149A	-2.34	SELS	-2.36	A_32_P142363	-2.38	THC2688475	-2.40
SLC30A7	-2.34	C11orf41	-2.36	CHMP2B	-2.38	DCAF4	-2.40
SERPINB8	-2.34	CYCS	-2.36	A_24_P821988	-2.38	UBTF	-2.41
OXNAD1	-2.34	PRKCA	-2.36	ABCA2	-2.39	MTAP	-2.41
CLCN6	-2.34	MLXIP	-2.36	ZNF365	-2.39	FAM59A	-2.41
C20orf46	-2.34	GOLM1	-2.36	TPM4	-2.39	RYR1	-2.41
THC2503819	-2.34	BRF2	-2.36	INPP5K	-2.39	THC2740750	-2.41
THC2504037	-2.34	PPP1R3F	-2.36	CRAMP1L	-2.39	AKAP11	-2.41
TSNARE1	-2.34	THC2562523	-2.36	C14orf118	-2.39	GOLGA8A	-2.41
AGAP7	-2.34	ENST00000369158	-2.37	FKBP10	-2.39	C14orf1	-2.41
NKAIN1	-2.34	AK092921	-2.37	FAM155B	-2.39	PCDHA1	-2.41
HIRA	-2.34	PRKAB1	-2.37	LPCAT1	-2.39	IER2	-2.41
PNMA2	-2.34	TTC21A	-2.37	SEC24C	-2.39	RAB7L1	-2.41
DDX31	-2.34	A_24_P625683	-2.37	EHD3	-2.39	LOC595101	-2.41
HIPK2	-2.34	LAMA1	-2.37	KCTD13	-2.39	BQ717518	-2.41
AK024926	-2.34	C3orf62	-2.37	THC2662244	-2.39	A_24_P238769	-2.41
PDCD6IP	-2.35	C19orf76	-2.37	PPFIBP2	-2.39	MEF2BNB-MEF2B	-2.41
MAFG	-2.35	COL1A2	-2.37	PRSS12	-2.39	ECM1	-2.41
SLC16A8	-2.35	THC2631150	-2.37	CELSR2	-2.39	FAM123A	-2.41
BRWD1	-2.35	GARNL3	-2.38	FLJ45340	-2.39	MAN2C1	-2.41
A_24_P204257	-2.35	SENP6	-2.38	MYO6	-2.39	A_24_P475115	-2.41
LOC100129196	-2.35	THC2734788	-2.38	A_32_P187245	-2.39	ZFAND2A	-2.41
ELOVL6	-2.35	GATA5	-2.38	SULT4A1	-2.39	HSD17B14	-2.41
ANKRD13D	-2.35	C10orf2	-2.38	PDGFA	-2.39	AK097166	-2.42
AK092508	-2.35	CPT1B	-2.38	GPR98	-2.39	DEM1	-2.42
THC2631248	-2.35	ZNF222	-2.38	ENST00000416851	-2.39	LANCL2	-2.42
PELO	-2.35	BC028243	-2.38	BQ188788	-2.40	TESK1	-2.42
GCGR	-2.35	BRD4	-2.38	MEIS3P1	-2.40	ANTXR1	-2.42
IFRD1	-2.36	CCDC113	-2.38	STMN3	-2.40	CT45A5	-2.42
ANKRD20A5P	-2.36	FDFT1	-2.38	ASCL2	-2.40	THC2543854	-2.42
VPS26B	-2.36	STK40	-2.38	REEP3	-2.40	CALCRL	-2.42

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SLC39A10	-2.42	STOX2	-2.44	A_23_P204225	-2.47	ZNF37A	-2.50
IVL	-2.42	AGRP	-2.44	MIR137HG	-2.47	EMILIN3	-2.51
METTL21A	-2.42	PDXDC2P	-2.45	FASN	-2.47	UAP1L1	-2.51
GOLGA8F	-2.42	MPPED1	-2.45	BRWD1	-2.47	FAM86C2P	-2.51
C11orf41	-2.42	CLDN5	-2.45	SLC16A9	-2.47	A_32_P12282	-2.51
ENST00000448014	-2.42	CYR61	-2.45	DNAH1	-2.47	PRRG1	-2.51
HDLBP	-2.42	ENST00000534720	-2.45	AF100640	-2.48	TMEM59L	-2.51
A_24_P940354	-2.42	INE1	-2.45	DMP1	-2.48	KLF6	-2.51
THC2664391	-2.42	CBLB	-2.45	SPAG9	-2.48	EVC	-2.51
FLJ45340	-2.42	TRPM3	-2.45	AK001108	-2.48	FGFBP3	-2.51
RGMB	-2.43	MAP1LC3A	-2.45	LOC653061	-2.48	A_32_P125185	-2.51
SH3BP5	-2.43	NPC2	-2.45	ALAS1	-2.48	FAM3C	-2.51
ARHGAP39	-2.43	USP7	-2.45	AF086376	-2.48	LOC388796	-2.51
HPX-2	-2.43	ZDHHC14	-2.45	TMEM155	-2.48	ISM2	-2.51
A_32_P79719	-2.43	ITPKC	-2.45	MAFK	-2.48	HLA-DPB1	-2.52
AK022609	-2.43	CEP104	-2.45	GNL1	-2.48	MED17	-2.52
SYCE3	-2.43	LOC643650	-2.45	SHOX2	-2.48	CYP27B1	-2.52
ERICH1	-2.43	ALDH1L1	-2.45	LRRK1	-2.48	A_24_P298179	-2.52
AK022183	-2.43	ITPRIPL2	-2.45	ZNF621	-2.48	X01147	-2.52
MAP9	-2.43	THC2750143	-2.45	ENST00000553378	-2.49	LOC648740	-2.52
BC036431	-2.43	CDKL5	-2.46	ZNF34	-2.49	FOSB	-2.52
LZTFL1	-2.43	ENST00000543840	-2.46	ASMTL	-2.49	TRPC3	-2.52
NFIL3	-2.43	THC2714457	-2.46	CCL19	-2.49	A_24_P933548	-2.52
GSDMA	-2.43	A_32_P134679	-2.46	CEBPA	-2.49	MICB	-2.52
THC2655811	-2.43	A_32_P184039	-2.46	BI836406	-2.49	KLHL2	-2.52
KRT80	-2.43	SRPRB	-2.46	A_32_P213103	-2.49	COLEC12	-2.52
HLA-DPA1	-2.43	RBMS3	-2.46	HAB1	-2.49	VPS53	-2.52
DYSF	-2.43	SOCS7	-2.46	A_24_P221668	-2.49	ARHGEF15	-2.52
CYP2E1	-2.44	SHC2	-2.46	ZMYND15	-2.50	REEP3	-2.52
SLC7A6	-2.44	TPM4	-2.46	CHPF2	-2.50	A_32_P73707	-2.53
ZNF506	-2.44	A_24_P187626	-2.47	A_32_P133821	-2.50	CAPN8	-2.53
THC2677432	-2.44	VMP1	-2.47	ITGAV	-2.50	RBM38	-2.53
GCLC	-2.44	CECR6	-2.47	A_24_P401090	-2.50	C4orf49	-2.53
THC2525188	-2.44	MMP16	-2.47	ENST00000532936	-2.50	ZNF791	-2.53
LHX6	-2.44	TPM4	-2.47	STX4	-2.50	KIAA0368	-2.53
AY429544	-2.44	MPP6	-2.47	A_24_P264416	-2.50	CNDP2	-2.53
STMN3	-2.44	PRNP	-2.47	PELO	-2.50	ARMCX3	-2.53
BX101288	-2.44	CHST10	-2.47	ANKS6	-2.50	ENST00000390243	-2.53
MAN2A2	-2.44	POU5F1	-2.47	AK091744	-2.50	PTH1R	-2.53
A_24_P461497	-2.44	BC031954	-2.47	A_32_P178537	-2.50	TWIST2	-2.54
LDLRAD3	-2.44					KIAA1875	-2.54

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
LOC100133091	-2.54	MKRN9P	-2.57	SOX8	-2.60	MICB	-2.64
AK000707	-2.54	AK022407	-2.57	CCDC57	-2.60	PABPC1L	-2.64
RHOB	-2.54	ARHGEF10	-2.57	TGM7	-2.60	THC2701686	-2.64
A_32_P46112	-2.54	TACR2	-2.57	A_24_P315564	-2.60	GNG8	-2.64
THC2689802	-2.54	KCNN2	-2.57	AGAP7	-2.60	ROBO2	-2.64
NP111770	-2.54	CARD11	-2.57	HELB	-2.60	COL6A2	-2.64
POLR3E	-2.54	ENST00000421542	-2.58	AK027225	-2.60	STX4	-2.64
THC2710559	-2.54	LYSMD2	-2.58	FGFRL1	-2.61	SERPINI1	-2.64
C9orf167	-2.54	AK123861	-2.58	THC2563307	-2.61	KLF13	-2.64
LENG8	-2.55	CDC42SE1	-2.58	SF1	-2.61	TNFAIP2	-2.64
DENND2A	-2.55	FTH1	-2.58	XIST	-2.61	NR4A1	-2.64
LRRC8B	-2.55	FLJ26850	-2.58	AOC3	-2.61	FAM3C	-2.64
CYP2D6	-2.55	ERICH1	-2.58	THC2718728	-2.61	AUTS2	-2.64
TMEM185B	-2.55	EIF3F	-2.58	A_24_P92771	-2.61	BATF3	-2.64
EYA4	-2.55	GFOD1	-2.58	IER2	-2.61	CR748243	-2.65
DPYSL3	-2.55	PLG	-2.58	A_24_P161393	-2.61	C14orf79	-2.65
SLC22A15	-2.55	LOC440792	-2.58	FAM151A	-2.61	BC001335	-2.65
ENST00000413768	-2.55	BC004503	-2.58	A_23_P314024	-2.61	SMAP2	-2.65
CHRDL1	-2.55	AR	-2.59	EVL	-2.61	DKFZp761E198	-2.65
NDUFAF4	-2.56	GCG	-2.59	THC2519365	-2.62	B4GALNT1	-2.65
THC2515382	-2.56	NEU1	-2.59	FAM120AOS	-2.62	CRTC3	-2.65
BC013295	-2.56	LOC100130331	-2.59	ZDHHC9	-2.62	USP31	-2.65
MMP16	-2.56	LOC100129033	-2.59	HIVEP1	-2.62	UBAP1L	-2.65
RASSF2	-2.56	RNF157	-2.59	GOLGA8F	-2.62	DIEXF	-2.65
THC2520478	-2.56	MYO1C	-2.59	THC2536659	-2.62	GLA	-2.65
AK090407	-2.56	BC013077	-2.59	NFKB2	-2.62	PCYT1B	-2.65
C12orf70	-2.56	LRG1	-2.59	ACTC1	-2.62	AF264627	-2.65
SOLH	-2.56	MLYCD	-2.59	SOSTDC1	-2.62	DCAKD	-2.66
INPP5K	-2.56	NR1D2	-2.59	FTH1	-2.63	DOK3	-2.66
ADAMTS13	-2.56	KLF6	-2.59	TGFBR2	-2.63	A_24_P290109	-2.66
RSU1	-2.56	NS3BP	-2.59	IQSEC1	-2.63	CACHD1	-2.66
SHISA3	-2.56	SETD5	-2.59	NIPA1	-2.63	BDNF	-2.66
LOC643802	-2.56	IDUA	-2.59	MUC20	-2.63	MAFG	-2.66
PTPRJ	-2.56	UNKL	-2.59	SYT15	-2.63	SYT15	-2.66
ZNF704	-2.56	FLCN	-2.59	SMAGP	-2.63	THC2667666	-2.66
A_32_P173922	-2.57	PDXDC2P	-2.60	ADAMTS7	-2.63	RNF145	-2.66
SAP30L	-2.57	PRLHR	-2.60	SLC19A2	-2.63	ACTR3BP2	-2.66
EPB41L4B	-2.57	AF088004	-2.60	A_24_P255786	-2.63	TSEN54	-2.66
ANKRD34B	-2.57	KCNJ14	-2.60	WWTR1	-2.63	AQP1	-2.66
INHBA	-2.57	SLC17A5	-2.60	THC2724111	-2.63	GOLGA8IP	-2.66
GOLGB1	-2.57	THC2517566	-2.60	PER2	-2.63	BI497361	-2.67

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
LPP	-2.67	IL15RA	-2.70	CB529149	-2.75	MAP3K1	-2.80
TRIO	-2.67	PGCP	-2.70	NXPH4	-2.75	LZTFL1	-2.80
HBEGF	-2.67	A_24_P49800	-2.70	A_23_P64962	-2.75	AF264621	-2.80
LAT	-2.67	C11orf96	-2.70	C3orf75	-2.75	GRIK3	-2.80
PARVA	-2.67	NAB2	-2.71	JHDM1D	-2.75	TMEM27	-2.80
ADAMTSL2	-2.67	A_32_P134556	-2.71	FAM89A	-2.75	KIAA1257	-2.80
SYT15	-2.67	TMEM130	-2.71	A_32_P89480	-2.75	BRD2	-2.81
SYNJ2	-2.67	MAN2C1	-2.71	UBQLN4	-2.75	A_24_P152974	-2.81
ATP2B1	-2.68	EMX1	-2.71	IDI1	-2.76	BM678681	-2.81
MAP9	-2.68	TMEM41B	-2.71	RECQL5	-2.76	ENST00000255403	-2.81
FUNDC2	-2.68	BGN	-2.71	BC030094	-2.76	POM121	-2.81
PANK2	-2.68	A_32_P60687	-2.72	C4orf32	-2.76	GPR135	-2.81
FILIP1L	-2.68	SOCS7	-2.72	A_24_P565503	-2.76	LGI2	-2.81
BF677084	-2.68	SYTL5	-2.72	HABP4	-2.76	AK022892	-2.81
RSL1D1	-2.68	ADARB1	-2.72	GPR137B	-2.76	MMP10	-2.81
A_24_P924739	-2.68	RBM19	-2.72	HSD17B7	-2.76	CYP2B6	-2.81
BX476711	-2.68	A_24_P584936	-2.72	HOXC8	-2.76	SPACA1	-2.81
GRIK1	-2.68	JUNB	-2.72	TDRD3	-2.77	BEND7	-2.81
ENST00000449958	-2.68	STX3	-2.72	UCP3	-2.77	A_24_P32215	-2.82
RHCE	-2.68	MICA	-2.73	SCD	-2.77	CLEC18B	-2.82
MUC5AC	-2.68	MAPT	-2.73	A_24_P585660	-2.77	CYP51A1	-2.82
KIAA0930	-2.68	NP113399	-2.73	NEFL	-2.77	A_24_P682550	-2.82
HSD17B7	-2.69	MUC2	-2.73	OPTN	-2.77	PLA2G4F	-2.82
A_24_P477610	-2.69	ENST00000541329	-2.73	TMEFF2	-2.77	STXBP6	-2.82
KIAA1462	-2.69	MUC3A	-2.73	DOCK9	-2.78	CASK	-2.82
DDX31	-2.69	PPAN-P2RY11	-2.73	NPC1	-2.78	HSPA14	-2.83
CX165016	-2.69	CHCHD7	-2.73	NMI	-2.78	W22487	-2.83
GUCA1A	-2.69	C16orf79	-2.73	THC2660977	-2.79	PHF8	-2.83
CB987747	-2.69	NFAT5	-2.73	A_24_P715434	-2.79	FIBCD1	-2.83
KAZN	-2.69	STOX2	-2.73	IL6R	-2.79	TMEM158	-2.83
ENST00000331856	-2.69	THC2685727	-2.73	ZNF500	-2.79	CCDC78	-2.84
TMEM150A	-2.69	ISPD	-2.73	A_32_P215404	-2.79	FBXL16	-2.84
AK022044	-2.69	AK074670	-2.74	TXNRD1	-2.79	PADI4	-2.84
TTYH2	-2.70	TRIB3	-2.74	A_24_P401521	-2.79	HOXB9	-2.84
PCNXL2	-2.70	A_24_P321184	-2.74	LGI4	-2.79	ITPRIPL2	-2.84
A_24_P350252	-2.70	IGLON5	-2.74	FGB	-2.79	FHIT	-2.84
FAM3C	-2.70	KIAA1377	-2.74	A_32_P82179	-2.79	STYK1	-2.84
SPTBN5	-2.70	ACTR5	-2.74	ZFHX3	-2.80	ZIC1	-2.84
A_24_P499481	-2.70	CAST	-2.74	THC2688123	-2.80	CCKBR	-2.85
A_24_P934971	-2.70	THC2663797	-2.75	TMEM87B	-2.80	A_32_P161140	-2.85
		ZFP28	-2.75	A_32_P121978	-2.80	A_24_P33403	-2.85

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
FAM155A	-2.85	LDLR	-2.91	JUNB	-2.97	ASPHD2	-3.02
LPP	-2.85	EFHB	-2.91	DUSP5	-2.97	HLA-H	-3.02
ZYX	-2.85	C17orf76	-2.91	SPRR2C	-2.98	HIPK2	-3.02
A_24_P33105	-2.85	HLA-A	-2.92	ENST00000424931	-2.98	BC009353	-3.02
SPDYE5	-2.86	A_24_P101879	-2.92	HSD17B7	-2.98	THC2719403	-3.02
THC2521437	-2.86	A_24_P264413	-2.92	DENND4A	-2.98	THC2708710	-3.03
A_24_P552677	-2.86	FLJ90757	-2.92	GALNT3	-2.98	DCLK2	-3.03
GLIPR1	-2.86	SRP19	-2.92	CRLF1	-2.98	USP27X	-3.03
DNPEP	-2.86	CLIP2	-2.92	A_23_P139166	-2.98	AV682647	-3.03
THC2565608	-2.86	AF010144	-2.92	A_32_P179807	-2.99	AK021824	-3.03
THC2666687	-2.86	ZDHHC11	-2.92	RPL23AP32	-2.99	EEF1D	-3.03
BX537819	-2.86	C4orf32	-2.93	AK090499	-2.99	PPAP2B	-3.04
NOS2	-2.87	AV650911	-2.93	A_32_P13442	-2.99	S72422	-3.04
AL521247	-2.87	CEBPB	-2.93	CORO2B	-3.00	ZNF222	-3.04
XKR6	-2.87	THC2687779	-2.93	CCDC149	-3.00	ITPR1	-3.04
KIAA1549	-2.87	C8orf68	-2.93	BF207040	-3.00	TCTE3	-3.05
CAMKK1	-2.87	REPS2	-2.93	UBL4B	-3.00	TBX6	-3.05
C3orf51	-2.87	NFATC1	-2.93	THC2541642	-3.00	AL134462	-3.05
A_24_P650011	-2.88	HELB	-2.93	GGT7	-3.00	LPP	-3.05
RALGDS	-2.88	RALGDS	-2.93	FTH1	-3.00	RFPL1-AS1	-3.05
ZDHHC14	-2.88	AL832820	-2.94	AK097166	-3.00	THC2568627	-3.05
MYC	-2.88	REEP3	-2.94	FGF7	-3.00	ITM2A	-3.05
CMTM7	-2.88	AI669333	-2.94	SLCO4A1	-3.00	DPYSL4	-3.05
ENST00000340695	-2.88	HIST2H2BE	-2.94	CRY2	-3.00	A_24_P230100	-3.05
AK074696	-2.88	RRP12	-2.94	NPIP	-3.00	CPEB1	-3.05
LOC157562	-2.88	ELP2	-2.95	TRPV1	-3.01	C6orf168	-3.06
LMF1	-2.88	C17orf51	-2.95	DUSP13	-3.01	C15orf5	-3.06
THC2635921	-2.89	REEP3	-2.95	TNC	-3.01	A_24_P869138	-3.06
ZNF783	-2.89	CYP51A1	-2.95	GNAI1	-3.01	SREBF2	-3.07
A_24_P400702	-2.89	DUSP2	-2.95	PNMA3	-3.01	HSPA6	-3.07
STMN3	-2.89	RET	-2.96	NECAP1	-3.01	ARHGAP32	-3.07
NFASC	-2.89	SLC2A13	-2.96	AK091057	-3.01	NAP1L3	-3.07
SLC9B2	-2.89	TAS2R14	-2.96	TBC1D3B	-3.01	SPHK1	-3.08
A_23_P8812	-2.89	THBS1	-2.96	KCNQ1OT1	-3.01	A_32_P100475	-3.08
CAMK2N1	-2.89	ARHGAP30	-2.96	FLJ42627	-3.01	TLL2	-3.08
LPIN1	-2.90	BM695552	-2.96	GLB1L2	-3.01	GOLGA8A	-3.08
A_24_P925808	-2.90	B4GALNT1	-2.96	SIRPA	-3.01	FTHL17	-3.09
GOLGA6A	-2.90	ENST00000515814	-2.96	A_23_P147404	-3.01	IFNAR2	-3.09
POU4F1	-2.90	AM181370	-2.97	C14orf79	-3.02	ETNK2	-3.09
GNRHR2	-2.91	CRNDE	-2.97	BM928667	-3.02	CEACAM1	-3.09
MMAB	-2.91	PLXNA1	-2.97	CU690321	-3.02	C19orf28	-3.10

Appendix II Gene Expression Changes in $A2780_{CBN-CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
AK123066	-3.10	SULF2	-3.17	OGT	-3.24	THC2614203	-3.31
BCO2	-3.10	ARMC9	-3.17	SLC30A3	-3.24	GAD1	-3.31
AP3B2	-3.10	BC040048	-3.18	PRND	-3.24	TP53AIP1	-3.32
CEACAM21	-3.10	U72516	-3.18	SIRPA	-3.24	A_32_P40673	-3.32
ACBD7	-3.10	AK022183	-3.18	NFAT5	-3.24	C2orf83	-3.32
ENST00000422481	-3.10	PAQR9	-3.19	TUBA4A	-3.25	LONRF1	-3.32
CFLAR	-3.11	A_32_P31580	-3.19	NAB2	-3.25	HES1	-3.32
COL4A5	-3.11	ZNF182	-3.19	GCLM	-3.26	MUCL1	-3.33
COL7A1	-3.11	ENST00000445770	-3.19	CCL27	-3.26	THSD1	-3.33
A_24_P915634	-3.11	PRAMEF8	-3.19	A_32_P50508	-3.27	GRIN3A	-3.33
AF090890	-3.11	C21orf96	-3.19	AK094726	-3.27	GCLM	-3.33
LOC148709	-3.11	SLC13A3	-3.19	RTN1	-3.27	FLJ31485	-3.33
ATP6V0D2	-3.11	TBC1D30	-3.19	MYCBPAP	-3.27	HOXB6	-3.33
A_24_P597242	-3.12	C3orf62	-3.20	LOC643837	-3.27	ZNF502	-3.33
PVR	-3.12	THC2484716	-3.20	CB854743	-3.28	MADCAM1	-3.34
THC2741548	-3.12	AB014766	-3.20	MAGEC1	-3.28	A_32_P32876	-3.34
STXBP6	-3.12	MMAB	-3.21	ZNF826P	-3.28	CD3E	-3.34
GPR172B	-3.12	NIPA1	-3.21	TRIB3	-3.28	GNPDA1	-3.34
BC034930	-3.13	SHC1	-3.21	ANXA8L2	-3.28	ADCY1	-3.35
A_24_P489649	-3.13	CU678847	-3.21	DPY19L2P4	-3.28	BM475547	-3.36
AK093691	-3.13	TOM1L2	-3.21	THC2703681	-3.28	PRSS47	-3.36
ZIC1	-3.13	TRPM3	-3.21	AF075112	-3.28	KLC1	-3.36
SQLE	-3.13	AKNA	-3.21	A_32_P1841	-3.28	AF026246	-3.37
BC030138	-3.13	BX647619	-3.21	SMAGP	-3.28	SMAP2	-3.37
SFTPA1	-3.13	C14orf79	-3.21	A_32_P149416	-3.29	WNT5B	-3.38
THC2650423	-3.14	IRX6	-3.21	CRYM	-3.29	MFHAS1	-3.38
THC2712372	-3.14	ZBTB1	-3.21	GGT7	-3.29	OTOA	-3.38
SCD	-3.14	A_24_P502660	-3.22	HES6	-3.29	DUSP2	-3.38
SOX7	-3.14	TTLL11	-3.22	ELL2	-3.29	THC2529512	-3.38
A_24_P916853	-3.14	TNFRSF9	-3.22	A_23_P421323	-3.30	LOC100506571	-3.38
LHFP	-3.14	KCNV2	-3.23	LOC729680	-3.30	HNF4A	-3.39
PPP1R15A	-3.15	C17orf74	-3.23	TTC17	-3.30	A_32_P201976	-3.39
LPP	-3.15	ENST00000398878	-3.23	GOLGA8E	-3.30	MYO1E	-3.39
CCPG1	-3.15	THC2739159	-3.23	ATAD3B	-3.30	THC2726959	-3.39
INPP1	-3.15	THC2621771	-3.23	A_32_P60632	-3.30	FAM129A	-3.40
AL390214	-3.16	ITGAV	-3.23	A_24_P749080	-3.30	ELOVL5	-3.40
SLC24A4	-3.16	ENST00000474213	-3.24	HIST2H2AA4	-3.30	ZNF684	-3.40
HES2	-3.16	NPPC	-3.24	A_24_P853366	-3.31	LONRF1	-3.41
BSN	-3.16	LOC100505915	-3.24	AF116616	-3.31	LOC151009	-3.41
THC2681437	-3.16	IDI2-AS1	-3.24	CPA4	-3.31	A_32_P116153	-3.41
GPR27	-3.17			ETS2	-3.31	DOCK4	-3.41

Appendix II Gene Expression Changes in $A2780_{CBN-CC}$ vs. $A2780_{CBN}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
TRIOBP	-3.41	BX537816	-3.51	CREB3L3	-3.61	LOC100505695	-3.79
FOXC1	-3.43	DB534761	-3.51	ASPHD2	-3.61	THC2650352	-3.79
PHLDA2	-3.43	C19orf6	-3.51	SREBF2	-3.61	MALAT1	-3.79
DOCK4	-3.43	WNK4	-3.51	GABARAPL1	-3.61	A_23_P119407	-3.80
CR606969	-3.43	ENST00000517562	-3.51	PLAG1	-3.61	MUC5B	-3.81
THC2650022	-3.43	PHLDA1	-3.52	C1orf226	-3.62	CLIP4	-3.81
C14orf49	-3.44	SCD	-3.52	A_32_P157471	-3.63	KLHL14	-3.82
RIMBP2	-3.44	LOC157627	-3.53	KIRREL3	-3.63	GPX3	-3.82
LARGE	-3.44	BC035156	-3.53	LOC284242	-3.63	AV701505	-3.82
ENST00000439362	-3.44	NFYA	-3.53	ENDOV	-3.64	RAB20	-3.83
S81524	-3.44	LDLR	-3.54	LOC643837	-3.65	A_23_P72252	-3.83
TTC22	-3.45	AK055679	-3.54	RRAGB	-3.65	TRIM7	-3.83
PCDH1	-3.45	MALAT1	-3.55	SGK223	-3.65	MGAT5B	-3.83
FHOD3	-3.45	ENST00000446232	-3.55	CISH	-3.65	PRSS23	-3.84
KLF10	-3.46	CPA5	-3.55	AB007953	-3.66	ENST00000360902	-3.85
RIPPLY2	-3.46	ATRNL1	-3.55	ARHGAP44	-3.66	ENST00000390323	-3.85
NIPAL2	-3.46	CYP26B1	-3.56	A_24_P928119	-3.66	ENST00000531225	-3.85
THC2537721	-3.47	C7orf54	-3.56	NPTX1	-3.66	AL049390	-3.85
LHX6	-3.47	NP414419	-3.56	ANKRD33B	-3.67	TNFRSF21	-3.86
KCNMA1	-3.47	A_24_P578445	-3.56	PLGLB1	-3.67	GABARAPL1	-3.86
KIF26B	-3.47	OSGIN1	-3.56	THC2701140	-3.67	LINC00301	-3.86
LRP8	-3.47	GBP1	-3.56	FOXA3	-3.68	SPDYE2	-3.87
FN1	-3.47	DPYD	-3.57	DNAH2	-3.69	HIST2H2AA4	-3.87
CDK20	-3.47	MAP6	-3.57	GGT7	-3.71	FNDC3B	-3.87
SETD5	-3.47	IL1R1	-3.57	ATL1	-3.72	TXNL1	-3.87
SARM1	-3.48	FJX1	-3.57	DHCR7	-3.72	A_32_P142664	-3.88
SHC1	-3.48	LOC286272	-3.57	MTNR1A	-3.73	LONRF1	-3.88
ANXA5	-3.48	A_32_P212566	-3.58	RUNX2	-3.73	AL137705	-3.88
AL109784	-3.48	MYL3	-3.58	ZNF93	-3.73	TRPM3	-3.88
SP100	-3.48	COL5A1	-3.59	MARCKS	-3.74	ENST00000423269	-3.88
LOC643401	-3.49	NECAB2	-3.59	NR4A3	-3.74	ENST00000537552	-3.90
ZDHHC11	-3.49	JUN	-3.59	ADAMTS17	-3.74	SRGAP1	-3.90
ETS2	-3.49	LOC286382	-3.59	A_32_P150269	-3.74	TMEM87B	-3.90
CCPG1	-3.49	MASP2	-3.59	OR7E91P	-3.74	RFPL3-AS1	-3.91
HOXD3	-3.49	CCNT1	-3.59	C11orf44	-3.74	GJB4	-3.91
SIGLEC5	-3.49	TMEM41B	-3.59	GABRQ	-3.75	SSFA2	-3.92
FPGS	-3.49	SRXN1	-3.60	IL17D	-3.75	THC2678309	-3.92
LONRF1	-3.50	THC2729109	-3.60	CA12	-3.75	PPP2R2C	-3.93
BACE2	-3.50	HUS1B	-3.60	KDM6B	-3.76	CD59	-3.93
GNLY	-3.50	MALAT1	-3.61	GOLGA6A	-3.77		
MPO	-3.51			BHLHE40	-3.78		

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
THC2636529	-3.93	A_24_P332911	-4.12	GBP1	-4.31	LPIN1	-4.57
A_23_P57836	-3.94	THC2624360	-4.12	BDNF	-4.32	POM121L8P	-4.57
MALAT1	-3.94	BCL2L11	-4.12	USP6	-4.32	GOLGA6L6	-4.59
LRRC4C	-3.94	PI16	-4.13	AGTR1	-4.33	TSPAN7	-4.59
TAS2R19	-3.94	CAST	-4.14	XK	-4.34	A_24_P7494	-4.59
DUSP8	-3.95	A_24_P565496	-4.14	CACNA1B	-4.35	NEAT1	-4.60
CBLN2	-3.95	NP450512	-4.15	LOC284454	-4.36	NECAB1	-4.63
FAM129A	-3.95	LOC100505915	-4.15	FOXC1	-4.37	EL953211	-4.64
STARD4	-3.95	PANX2	-4.16	BX091616	-4.37	BU618641	-4.64
A_32_P125736	-3.97	AK124352	-4.16	XCL2	-4.38	BC037919	-4.64
THC2653489	-3.97	A_24_P911306	-4.16	AK024602	-4.38	INSIG1	-4.64
SLC45A4	-3.97	MAFIP	-4.17	THBD	-4.38	C9orf47	-4.66
CLDN17	-3.97	CHST2	-4.17	LZTS1	-4.39	HIC1	-4.66
AK027319	-3.97	A_24_P148263	-4.18	DDIT3	-4.39	FAM19A4	-4.66
ZNF263	-3.98	EMILIN2	-4.18	BX113029	-4.40	BX112754	-4.68
RBM14	-3.98	EFS	-4.18	TRIB1	-4.40	PRSS23	-4.68
SPACA3	-3.99	KIAA1654	-4.19	ATF3	-4.41	ADAM23	-4.68
DCAF4L2	-4.00	KCNC1	-4.19	NGLY1	-4.41	BG682198	-4.69
XM_001714359	-4.00	EMILIN1	-4.20	AY227436	-4.41	ENST00000553312	-4.70
CCPG1	-4.00	ENST00000538590	-4.20	PAX4	-4.41	HMGCR	-4.70
C17orf108	-4.01	C15orf50	-4.22	SC5DL	-4.42	RAB3C	-4.72
A_24_P1873	-4.02	ZDHHC22	-4.23	ENST00000333156	-4.43	DHCR24	-4.74
SYF2	-4.02	THC2737770	-4.23	A_32_P121483	-4.43	LGALS12	-4.75
HTRA1	-4.02	ARL10	-4.24	LY6G5C	-4.44	AK022268	-4.75
DLX3	-4.03	MAGEL2	-4.25	THC2708422	-4.44	LOC400794	-4.75
SIRPG	-4.03	HGSNAT	-4.25	AF088007	-4.44	BC029452	-4.75
A_24_P857002	-4.04	DLEC1	-4.26	UST	-4.44	ARPC4-TTLL3	-4.76
MYOZ3	-4.04	LOC285141	-4.26	KBTBD8	-4.45	FOSL1	-4.76
PLA2G2F	-4.06	TRPM3	-4.27	SERPINE1	-4.46	XKR4	-4.77
A_23_P73096	-4.06	CYP7B1	-4.27	GLYAT	-4.47	ATP10A	-4.80
LOC497257	-4.06	AMIGO2	-4.28	ARHGEF2	-4.49	THC2643957	-4.81
AK024382	-4.08	ONECUT2	-4.28	SSFA2	-4.50	ZDHHC9	-4.82
TMEM200C	-4.08	KCTD12	-4.28	AK123096	-4.52	PNPLA3	-4.82
B4GALNT3	-4.09	BC034271	-4.28	ANTXR2	-4.53	MANEAL	-4.82
LRP8	-4.09	HLA-DPA1	-4.29	SLCO5A1	-4.53	A_24_P935852	-4.82
U88896	-4.10	AJ004954	-4.29	BC069659	-4.54	BICC1	-4.83
TMEM87B	-4.11	BC037919	-4.30	TNFRSF12A	-4.54	HLA-DMA	-4.84
LOC284454	-4.11	CSAG1	-4.31	LOC439949	-4.54	GALNTL4	-4.84
A_24_P678056	-4.11	LOC100507780	-4.31	BACE2	-4.54	COL1A1	-4.84
GABARAPL3	-4.11	AF007193	-4.31	GPC5	-4.55	POMC	-4.85
ENST00000412063	-4.12	A_24_P238819	-4.31	SCD	-4.56	C15orf2	-4.85

Appendix II Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CBN}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
MIR22HG	-4.85	THC2655842	-5.14	KLHL29	-5.62	LONRF2	-6.28
FOXF2	-4.85	HLA-DMA	-5.15	FOXD4	-5.63	ENST00000390539	-6.28
A_24_P409182	-4.86	FAT1	-5.16	AF222023	-5.64	RASD2	-6.28
A_24_P383199	-4.88	SERPINA10	-5.17	FOXO1	-5.66	AW627629	-6.29
KIF5C	-4.88	FZD8	-5.17	EXT1	-5.68	C22orf31	-6.29
KIR2DS4	-4.89	MAP3K14	-5.18	DACT1	-5.72	TMCC2	-6.31
LINC00304	-4.90	FOS	-5.18	THC2661428	-5.75	ARL10	-6.34
THC2674306	-4.90	CD177	-5.18	P2RX1	-5.76	THC2535753	-6.36
ADARB1	-4.90	SC5DL	-5.20	A_24_P281514	-5.76	HMGCS1	-6.40
TCF23	-4.91	RGS16	-5.20	AK021593	-5.76	LOC729652	-6.44
DHCR24	-4.91	LPP	-5.20	ARHGAP31	-5.76	LAMP3	-6.45
ENST00000544461	-4.91	AF010144	-5.21	LRFN5	-5.78	BC062473	-6.45
ENST00000439259	-4.91	HIF3A	-5.21	D16474	-5.79	EID3	-6.45
CLN8	-4.92	LOC388630	-5.22	THC2710703	-5.79	PRDM7	-6.51
NT5DC3	-4.92	A_23_P46070	-5.23	ABP1	-5.79	A_24_P452024	-6.53
BG428517	-4.93	A_32_P213543	-5.24	DUSP8	-5.82	ARHGAP31	-6.54
MSMO1	-4.93	ZNF642	-5.24	A_24_P587993	-5.85	SPARCL1	-6.55
HIC1	-4.95	GNAZ	-5.25	THC2642650	-5.86	THC2654993	-6.58
THC2560073	-4.95	THC2677037	-5.31	AF116619	-5.87	BC031314	-6.59
IL12A	-4.95	LY9	-5.32	REXO1L1	-5.89	PCDHB9	-6.60
RGS16	-4.95	AGPAT9	-5.34	FAM196A	-5.90	CROCCP3	-6.63
EPAS1	-4.95	PLGLB1	-5.35	ENST00000182096	-5.93	TSC22D3	-6.64
C14orf37	-4.95	BEST3	-5.40	A_32_P73717	-5.96	THC2687042	-6.64
ENST00000417781	-4.96	A_24_P492919	-5.43	LOC100505880	-5.97	A_24_P940079	-6.65
C6orf145	-4.97	CCR3	-5.43	TNFAIP8L3	-5.97	TGFBI	-6.68
KLHL6	-4.97	THC2654921	-5.44	KIAA0319	-5.98	UPK3A	-6.69
AL834280	-4.97	AF257098	-5.44	A_23_P141785	-5.98	CCDC48	-6.69
AK054921	-4.99	RGMA	-5.45	BICD1	-5.99	PLVAP	-6.72
LOC100127983	-5.00	SPATA13	-5.46	BEGAIN	-5.99	SSFA2	-6.73
A_24_P928453	-5.01	C9orf150	-5.47	SQSTM1	-6.02	LOC653061	-6.79
THC2698892	-5.01	DPYD	-5.47	FOSL1	-6.06	A_23_P251002	-6.80
LOC100652749	-5.02	SLC45A1	-5.48	AI911586	-6.07	TDRD10	-6.84
CLN8	-5.04	CASC2	-5.51	ENST00000443034	-6.08	PFKFB3	-6.85
THC2487011	-5.05	THC2740861	-5.51	FAM153A	-6.09	CEACAM19	-6.87
NXPH4	-5.07	KCNJ1	-5.51	A_32_P220912	-6.10	SRPX	-6.88
KIAA0319	-5.08	DHX34	-5.52	GNG13	-6.12	AMZ2P1	-6.89
BQ674642	-5.09	RUFY2	-5.55	THC2701422	-6.14	MAFF	-6.90
THC2677796	-5.11	COL5A1	-5.56	ARMCX2	-6.16	PDZRN3	-6.93
SPAG9	-5.13	TSPAN32	-5.56	EFHC2	-6.27	ENST00000485253	-6.97
AK022140	-5.13	ENST00000361201	-5.58	A_32_P141938	-6.27	A_24_P315885	-7.07
		A_32_P146450	-5.59				

Appendix II Gene Expression Changes in $A2780_{CBN-CC}$ vs. $A2780_{CBN}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
AK022044	-7.07	FSTL5	-9.09	SPP1	-22.23		
OTUD1	-7.09	JAKMIP1	-9.37	IRS2	-22.51		
HES1	-7.09	TRIM9	-9.56	PTPN3	-25.20		
HOXA2	-7.14	A_23_P393495	-9.62	TAC1	-25.64		
HMGCS1	-7.16	MDGA1	-9.87	HTRA3	-25.68		
RFTN1	-7.18	KIAA1751	-10.06	LIPG	-26.45		
SC5DL	-7.18	BAI3	-10.14	EGR3	-27.78		
TNFRSF21	-7.20	HSPA12A	-10.15	EGR2	-29.16		
KBTBD11	-7.22	BIRC3	-10.23	ACSS1	-32.75		
THC2712687	-7.24	PPP3CA	-10.32	LIPG	-40.60		
THC2686110	-7.40	C3orf80	-10.38	TAC1	-60.77		
GRID1	-7.44	FAM46A	-10.84	LAMB1	-86.10		
ENST00000390636	-7.48	EPHA3	-10.93				
KAZN	-7.54	BAALC	-10.97				
CLN8	-7.55	MEST	-11.00				
RBM11	-7.57	NEFL	-11.36				
A_23_P108534	-7.61	ARC	-12.08				
LAMA1	-7.63	DACT1	-12.31				
A_32_P38821	-7.71	JAKMIP3	-12.55				
NPTX2	-7.74	PTPN3	-12.56				
ZNF469	-7.75	AK094289	-12.60				
IFI44	-7.85	LINC00421	-12.93				
A_24_P928031	-7.87	TSHZ3	-12.96				
A_24_P923510	-7.89	EPHA3	-12.99				
NEAT1	-7.97	IRX4	-13.28				
TSPAN8	-8.02	ENST00000318245	-13.62				
CELF6	-8.11	PLK2	-13.69				
BM926140	-8.23	GDF10	-14.36				
MKL2	-8.38	ODZ2	-14.59				
ENST00000518339	-8.39	EGR1	-15.82				
RELB	-8.43	EGR4	-16.33				
ST18	-8.47	ZDBF2	-16.50				
A_32_P138939	-8.57	LIF	-16.77				
F7	-8.73	KCNMA1	-17.16				
A_24_P746044	-8.75	PRDM13	-17.20				
ITGBL1	-8.89	A_23_P123234	-18.30				
ATF3	-8.90	GDF10	-18.87				
HIVEP3	-8.90	GPR84	-19.53				
A_24_P771821	-8.96	BEX2	-19.70				
AI732190	-9.04	HMOX1	-20.56				
		IGF2	-22.00				

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation $\geq$2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
GPM6A	1456.0	CCR1	142.64	MDFIC	69.11	PDGFRA	42.16
CXorf57	1155.5	PLEKHG4	141.22	NAALAD2	66.74	LCP1	41.74
RBMS3	1105.9	GLUL	138.43	MYOF	66.49	TLE4	41.50
RNF128	956.06	CRISPLD1	129.88	MARCKS	64.18	PAG1	41.11
SLC25A24	776.27	RFTN1	129.74	SLC16A3	61.06	CLDN8	40.95
CNRIP1	647.16	GRIK1	126.70	AK125162	60.78	ENST00000323496	40.88
MMP10	537.19	PDGFRB	125.17	TMEM98	59.94	FOXD1	40.82
TGFB2	461.12	PCDH15	121.82	KIAA2022	59.91	THC2753543	40.70
GALNT14	444.70	CBLB	119.58	ZNF704	58.39	TMSB4X	40.15
MUM1L1	419.83	MMP1	119.09	CYP1B1	58.17	GLT1D1	39.94
ANO3	384.93	A_24_P530977	117.63	NOX4	57.28	WIF1	39.92
NUDT10	384.12	ENST00000517562	115.79	MEOX2	56.60	SPG20	39.73
COLEC12	291.05	MMP16	115.04	IKZF2	56.13	FILIP1L	38.51
ENOX1	277.30	TMSB4X	111.50	SRPX	54.20	ZPLD1	38.17
LRRTM4	239.36	MBNL3	107.82	PAG1	53.00	NOS2	37.52
ZNF521	230.10	FOLH1B	102.58	LRRTM4	52.41	TMEM65	37.32
RBMS3	220.83	EYA4	96.47	SLIT2	52.27	CTSZ	36.79
TMSB15B	219.88	ITM2A	96.15	KIF26B	51.93	LRFN5	36.67
TMEM47	192.27	TMSB4X	95.30	TCEAL6	51.29	NUDT11	35.22
DUSP6	189.07	SPG20	92.85	TGFBR2	51.04	FBXL7	34.06
A_32_P106615	178.39	ZNF704	90.58	RNF128	49.73	SLC22A15	34.03
EYA4	174.42	BC028039	88.20	ZFHX4	49.71	PI15	33.85
EMP1	171.78	TTC39C	88.06	AUTS2	49.32	FOLH1	32.56
NRIP1	168.04	LRRTM4	86.38	C1orf21	48.94	F2R	32.23
TMEM98	148.35	NOX4	84.53	C11orf41	48.31	ALDH1A3	32.11
SPATS2L	145.31	EGR2	84.33	DPYSL5	47.78	LACC1	32.03
EPDR1	144.39	TCEAL5	83.30	MAP1B	47.40	CHRDL1	31.96
		SATB1	81.03	PLXDC2	47.29	PLCE1	31.44
		TCEAL3	78.42	NEDD4L	47.17	ALCAM	31.35
		PDE9A	76.62	DPYSL2	46.96	TBC1D8B	31.30
		GJA1	75.37	BET3L	46.94	TRIML2	31.13
		AR	74.18	NUDT11	46.74	EPAS1	31.09
		BCL2	70.14	FAM129A	46.31	C11orf75	30.35
				ROBO2	46.00	BET3L	30.32
				DPYSL2	45.83	SYCP2	30.03
				RBMS3	45.20	RPRML	29.68
				MYOF	45.10	SCN9A	29.47
				MAP1B	44.50	COL1A1	29.04
				ENST00000419364	43.74	TLE4	28.05
				CYR61	42.36	LOC100127983	27.91
				INPP4B	42.19	TSPAN5	27.34

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
PNMA2	27.04	NEDD4L	22.12	WNT3A	18.34	CD302	15.68
BCL6	26.93	ETS2	22.04	MFAP4	18.15	NTF4	15.48
PREX1	26.81	OGFRL1	21.98	PRSS12	18.07	GBP1	15.38
CALB1	26.78	DISC1	21.77	THC2642212	17.93	DTNA	15.35
CYR61	26.68	ST3GAL6	21.62	PPIC	17.91	LOC100505971	15.28
SP110	26.64	GNG2	21.59	NMU	17.79	DNAJC22	15.16
EMILIN1	26.29	HIF3A	21.51	DDAH1	17.77	THC2717825	15.16
PLCL2	26.05	A_32_P68479	21.40	THC2729899	17.67	FAM84B	15.14
CSRNP3	25.90	GRASP	21.31	SYTL4	17.63	MECOM	15.03
SPARCL1	25.59	OLFML3	21.13	AK129542	17.38	FAM171B	15.02
GDF10	25.48	C4orf32	21.09	C2orf65	17.35	A_23_P421323	14.98
TSPAN5	25.44	PERP	21.06	LTBP1	17.18	PKNOX2	14.82
STXBP6	25.33	TCF7L1	21.03	WDR17	17.09	ANXA2	14.81
ZNF439	25.29	ATP6V0D2	20.87	FBLN5	16.87	FNDC1	14.80
ZNF613	24.95	FOXA1	20.80	WIPF1	16.87	RTKN2	14.56
RBMS3	24.79	EPB41L3	20.77	ENST00000428809	16.86	MBNL3	14.48
MUC15	24.63	SLC7A3	20.76	SDK2	16.78	MYOF	14.47
BX119882	24.49	TAC1	20.73	TMEM2	16.76	ARHGAP23	14.29
IQGAP2	24.46	ENST00000423704	20.70	FAM171B	16.74	PLCL2	14.14
DOCK3	24.17	CALCRL	20.62	NEO1	16.57	FLJ35024	14.09
TGFB2	24.07	PPIC	20.61	TRPC4	16.57	PODNL1	14.08
LOC100192378	24.06	A_32_P168756	20.58	DACT1	16.52	ZNRF2	14.07
SYCP2	24.04	MTSS1	20.48	HCG23	16.48	NUDT10	13.94
THC2681889	24.01	FHOD3	20.32	PRR16	16.39	LOC100128164	13.93
TTC39C	24.01	THC2732175	20.19	SEMA3C	16.36	C9orf93	13.88
STMN3	23.99	CD248	20.08	AMOTL1	16.29	ZNF469	13.82
RND3	23.72	PAX9	19.72	KIAA2022	16.20	TPBG	13.81
LOC644662	23.50	EOMES	19.68	LOC100127983	16.16	TBX15	13.75
APLF	23.34	FRY	19.62	EFNA5	16.13	ENST00000537659	13.75
LOC389634	23.31	MID2	19.21	ETV1	16.08	HOXB4	13.74
NAP1L2	23.17	MOB3B	19.17	MOCOS	16.06	NAP1L3	13.74
TMEM2	23.00	RNF150	18.85	BOD1L	16.00	LRRCC1	13.64
UTRN	22.43	PGCP	18.83	GBP1	15.94	AF363068	13.58
GPC5	22.31	GHR	18.73	HS6ST2	15.90	RASIP1	13.50
STXBP6	22.29	TUBB2B	18.58	MID1	15.85	TAC1	13.48
ESRRG	22.29	CCDC116	18.57	CHRDL2	15.83	TTC39C	13.46
POSTN	22.28	ETS2	18.55	RTN1	15.77	DA727827	13.43
KIAA1147	22.25	LOC647946	18.49	SULF1	15.71	CLMN	13.42
FES	22.23	LRRCC1	18.46	RNF144A	15.70	FIGN	13.35
METRNL	22.13	GRB14	18.38	SAMD13	15.69	PLOD2	13.34
SMPDL3A	22.13	TUBB3	18.37	RASGRP1	15.68	FAM43B	13.33

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
DB534761	13.24	BC015334	11.46	MXRA8	10.41	POU4F1	9.38
BG216262	13.18	THC2753396	11.41	THC2673973	10.35	XK	9.38
SH3BP4	13.15	ESX1	11.37	EPS8	10.33	MCAM	9.35
GATM	13.14	GALNTL1	11.35	TM4SF4	10.31	MCF2L-AS1	9.29
THC2657737	13.04	CYP26B1	11.35	SPAG1	10.27	MOXD1	9.26
MECOM	13.03	F2RL2	11.29	CXorf57	10.23	SLC10A4	9.26
GPRASP2	13.03	CR594811	11.28	A_23_P216071	10.18	FOXO1	9.15
LMO7	12.99	GRRP1	11.27	C12orf39	10.16	PTRF	9.14
BMP8B	12.97	MARK1	11.24	ENST00000449075	10.16	SLC7A7	9.13
CYR61	12.94	ANKRD45	11.22	A_32_P85379	10.15	ANGPTL2	9.11
PRR11	12.89	EGFR	11.20	AK055647	10.15	PRSS23	9.09
JAM2	12.88	PTPRD	11.20	BG428517	10.13	EGR1	9.03
PCDHA11	12.83	ARNT2	11.15	RBMS1	10.08	RFC3	8.97
THC2560357	12.79	LGR4	11.12	CHST11	10.04	ROBO2	8.96
FAM171B	12.78	FOXE1	11.11	RIPK2	10.01	THC2638839	8.94
UST	12.76	OLFML3	11.11	SVIL	10.01	GJA3	8.92
SCN7A	12.56	TSPAN9	11.05	CHST11	9.93	PGM2L1	8.91
OTX1	12.53	PARVA	10.92	ERI2	9.92	MTL5	8.91
LRRC8C	12.45	MOCOS	10.91	STAU2	9.92	KIF5C	8.85
BCAS4	12.44	SLIT2-IT1	10.88	WIF1	9.91	FOXD2	8.84
AK092875	12.42	COL16A1	10.88	LOC728392	9.90	TNNC1	8.83
MORC4	12.42	RORB	10.87	ANKRD43	9.89	SLC45A3	8.81
A_32_P331700	12.39	GNAI1	10.87	SCN9A	9.88	MCM3AP-AS1	8.72
RBMS1	12.36	AGAP2	10.86	STMN3	9.82	TFCP2L1	8.72
TMEM158	12.35	C8orf47	10.83	TMEM150C	9.82	NUAK1	8.68
GJA1	12.26	ADRA2C	10.77	IKZF2	9.76	LINC00312	8.67
LIMD2	12.24	AK024926	10.73	A_23_P384355	9.73	A_32_P90615	8.67
SEMA3D	12.23	GPR4	10.73	MAGI3	9.73	A_24_P914062	8.63
PTH1R	12.23	FAM198A	10.70	STRN	9.72	PMP22	8.60
PLAC9	12.12	MAGI3	10.65	MCF2L-AS1	9.70	TGFB1I1	8.58
ITGA6	12.01	ROBO2	10.63	PDGFA	9.68	CGNL1	8.58
ATP6V0D2	12.01	RTKN2	10.60	LIMD2	9.64	MAGEA2B	8.56
GDAP1	11.99	RPS6KA6	10.58	GLDC	9.64	PRKCA	8.48
HLA-DPB1	11.98	PRKCE	10.56	CD302	9.63	ADC	8.47
LARGE	11.94	FBXL16	10.54	NEDD4L	9.52	DFNB31	8.44
FCHO1	11.77	C11orf96	10.54	PHC1	9.52	MCF2L	8.41
LMCD1	11.75	A_24_P212997	10.47	ITGAV	9.50	TMSB15A	8.39
CD163	11.72	PARVA	10.46	LRMP	9.49	WIPF1	8.38
GEM	11.63	SOX7	10.46	SYT6	9.46	LINGO1	8.36
ST3GAL1	11.61	THC2755690	10.45	A_32_P327750	9.44	PARVA	8.36
IFIT1	11.55	TTC39C	10.42	THC2677011	9.40	C18orf1	8.36

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
A_32_P136304	8.34	C9orf93	7.52	SLC12A6	7.00	BG951379	6.63
LOX	8.33	CR598370	7.51	DIAPH3	6.98	BE881987	6.60
AP4E1	8.29	LOC202025	7.51	PRSS23	6.98	FAM122C	6.59
C4orf32	8.23	PLXNC1	7.50	HOXB13	6.96	AF038185	6.58
ZNF704	8.20	ENST00000551187	7.49	OSGIN2	6.95	SEPSECS	6.54
TRPM6	8.18	MID1	7.48	CPS1	6.95	PODNL1	6.54
KDSR	8.18	STAU2	7.47	CCDC40	6.94	RAB39	6.54
CGNL1	8.17	C19orf18	7.46	DKK3	6.92	CGN	6.54
RASSF4	8.17	CAPS2	7.46	SCN9A	6.91	SGTB	6.54
YBX2	8.15	ANXA2P3	7.45	LOC145757	6.90	NPPC	6.53
PHC1	8.14	AK094175	7.43	PTRF	6.89	KIAA1407	6.53
ENST00000551107	8.11	MBOAT2	7.42	LRRC16A	6.88	FOLH1	6.51
A_24_P229726	8.00	ENST00000550287	7.37	GAB1	6.87	XKR6	6.51
NXNL2	7.97	ARVCF	7.35	LOC84989	6.86	CLGN	6.50
SNX16	7.97	SNX16	7.35	BU602485	6.86	BQ933774	6.50
CSGALNACT1	7.96	KIF3C	7.34	TMSB4X	6.83	B4GALT6	6.49
THBS1	7.96	GAB2	7.31	EMP1	6.83	PRDM5	6.49
FOXE1	7.96	NIN	7.28	PAQR8	6.82	ETV4	6.48
CACNG7	7.95	SH3GL3	7.28	EIF5A2	6.82	CNTFR	6.48
PAQR5	7.95	MTBP	7.27	MME	6.80	NLGN3	6.48
DIAPH3	7.93	AUTS2	7.27	CLDN17	6.80	ZSCAN2	6.47
ENST00000505709	7.91	APC2	7.27	SOCS3	6.77	FXYD1	6.47
EDA	7.84	KCNC1	7.22	MXRA8	6.77	IGSF9	6.47
ETV1	7.81	LOC439911	7.21	TMEM30B	6.76	A_32_P136063	6.46
TBXAS1	7.80	TEX19	7.19	MIR17HG	6.76	MME	6.46
MCAM	7.79	WDHD1	7.19	ST8SIA5	6.76	RGS5	6.46
WDR17	7.79	LOC100505566	7.18	ACBD5	6.75	A2M	6.44
NECAB1	7.78	A_24_P917810	7.18	WDR65	6.75	ENST00000502419	6.43
FAM129A	7.77	TRIM9	7.17	HOXC13	6.74	CLEC11A	6.43
TSPAN7	7.75	C14orf167	7.12	ABCA1	6.74	A_24_P401051	6.41
HOXC12	7.72	GTF2A1	7.12	DHX40	6.74	FBXO16	6.40
FLVCR2	7.68	KIF16B	7.09	KLF6	6.72	SGOL1	6.39
DLX4	7.68	TCF4	7.08	FXYD5	6.70	ENST00000542925	6.39
ADAMTS4	7.63	JAM2	7.08	IFT81	6.69	ZNF273	6.38
MIR17HG	7.62	TMC6	7.07	LOC100506123	6.65	TOX2	6.37
X15674	7.62	FAM164A	7.07	PAX9	6.65	HMGN5	6.37
HMMR	7.55	A_32_P80697	7.04	ANTXR1	6.65	CLDN1	6.37
BC053880	7.55	CLMN	7.03	PAPPA	6.65	AMMECR1	6.35
GREB1	7.55	RNF182	7.02	NPAS2	6.65	MCART1	6.35
SOX7	7.54	GAS2L3	7.02	MMP3	6.64	SAMD14	6.33
				AK096104	6.64		

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
AK026750	6.32	A_24_P281264	6.03	KIAA1107	5.83	KCNA7	5.63
RAB9B	6.31	ENST00000513644	6.01	ABCG4	5.82	DIAPH3	5.63
RET	6.31	FBXO15	6.01	ANXA2	5.82	PLAU	5.61
TSPAN12	6.30	AL049990	6.01	CEP55	5.82	CASC5	5.61
CDKL5	6.29	OSBPL7	6.01	BRWD3	5.82	EPB41	5.61
TMEM159	6.29	BTN3A3	6.00	IGF2	5.82	TMPRSS5	5.61
EDNRA	6.29	PURG	6.00	CASC5	5.81	INPP4B	5.60
KLF2	6.26	KIAA1274	5.99	OCA2	5.81	LRRN3	5.60
RASSF2	6.23	LOC100499466	5.99	NFKBIZ	5.80	NEURL1B	5.60
A_32_P19797	6.23	AI056399	5.98	FLJ37035	5.80	PDP1	5.59
IL21R	6.22	SHF	5.98	GDF10	5.79	BDH2	5.59
ASAP2	6.21	CEP112	5.98	IL1RAPL2	5.78	TGFB3	5.58
MEIS3	6.20	UGT3A2	5.97	THC2672257	5.78	AB062488	5.58
THC2575678	6.18	KIAA1407	5.97	IL11	5.78	BX647792	5.58
NANOS3	6.18	PLAG1	5.95	INA	5.78	THC2681437	5.58
TDRD12	6.17	SLC6A6	5.95	GPRC5C	5.77	DUSP19	5.57
CASP7	6.17	TESC	5.94	RASSF5	5.77	SHROOM2	5.56
NAV1	6.16	JPH1	5.94	ENST00000537149	5.76	THC2596442	5.56
C18orf54	6.16	THC2682661	5.94	RBM24	5.76	EPS8L1	5.56
FZD8	6.14	KCNH2	5.94	ALPK2	5.76	CDH7	5.56
RALGPS2	6.13	FXYD5	5.93	BTNL9	5.75	VSIG10	5.56
EFR3B	6.12	SERPINE2	5.92	CACNA1C	5.75	ACYP2	5.55
TMEM130	6.12	C9orf95	5.92	NEDD4L	5.75	AK026418	5.55
STMN3	6.11	ATXN3	5.91	HSD17B11	5.75	ANXA2	5.54
GCLC	6.11	OTUD4	5.91	IL15	5.74	A_23_P123234	5.53
RIPK2	6.10	ENST00000431244	5.91	RAB9B	5.73	A_23_P91130	5.52
ENST00000461931	6.10	MAP7D2	5.90	SPHK1	5.70	SLC37A1	5.52
TLR3	6.09	CENPA	5.90	CDKN1C	5.69	LOC284454	5.51
A_32_P57717	6.08	CSPG4	5.90	CKLF	5.69	ENST00000525173	5.51
MAGI2	6.08	HHAT	5.89	FOXA1	5.68	ANXA2P1	5.51
C17orf67	6.08	TTLL7	5.89	DIAPH3	5.68	KIF11	5.49
AK123584	6.08	FAM102B	5.88	GLRX2	5.68	CSRNP1	5.49
CRLF1	6.07	DHRS2	5.88	FAM63A	5.68	SCD5	5.45
KIAA1377	6.07	HTRA1	5.86	LOC100505894	5.66	ATP2A3	5.45
NRG2	6.06	HOPX	5.86	CTAGE1	5.66	SPAG1	5.45
AP4E1	6.06	SPRED1	5.85	FJX1	5.65	SWT1	5.45
A_24_P178475	6.05	C12orf53	5.84	MGAT4A	5.65	AL574966	5.44
TGM2	6.05	KLF7	5.84	RAB3C	5.65	ATXN3	5.44
A_24_P281175	6.04	CHRNA7	5.83	CEP112	5.64	RALGPS2	5.43
APC2	6.04	A_24_P720495	5.83	MEIS3	5.64	LRRC10B	5.41
SRRM3	6.04			ACPL2	5.63	BM723547	5.41

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation $\geq$2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
TMEM200B	5.41	ABCD3	5.20	KIAA0226L	4.98	PRKCH	4.84
MMP16	5.41	HOXB6	5.20	A_32_P134679	4.98	CD47	4.83
RECQL	5.41	THC2707492	5.19	LOC440434	4.98	ENST00000456585	4.83
AK021664	5.41	SLC8A2	5.19	THC2703681	4.98	ADC	4.82
THC2559002	5.41	BOLA1	5.17	SPRED1	4.98	ANKRD36	4.82
ENST00000448494	5.40	KCNG1	5.17	TMEM87B	4.97	GAS2L3	4.82
FAM161A	5.40	GPRC5C	5.16	C1orf187	4.97	RTN4R	4.81
KCNA7	5.39	NUDT13	5.15	AMOT	4.96	A_32_P156628	4.81
STARD8	5.38	TEKT4P2	5.15	STARD13	4.96	RASSF4	4.81
IL4R	5.38	MRAP2	5.15	SYNE2	4.96	KIAA1211	4.80
HTN3	5.38	THC2493376	5.14	THC2666403	4.96	SMYD3	4.80
ACTL8	5.38	CV800149	5.14	PIK3CD	4.95	NR4A1	4.79
THC2656116	5.38	RGS16	5.14	SIX4	4.95	LRRC37A4	4.79
C21orf119	5.37	A_32_P93894	5.13	H19	4.94	CORO2A	4.79
CRYZ	5.36	KCNF1	5.13	ZNF826P	4.94	CARD10	4.79
LOC100270746	5.36	RBMS1	5.13	LMF1	4.94	EPN3	4.78
LACC1	5.35	SPIN4	5.12	TUBB8	4.94	VSIG10	4.78
STRN	5.35	OSBPL10	5.11	THC2699069	4.93	THC2717828	4.78
MDFIC	5.35	BPNT1	5.11	CHRDL2	4.93	LOC100652958	4.78
AA541413	5.34	RCOR3	5.11	DUSP27	4.93	S100A4	4.77
ETV4	5.33	TM4SF1	5.10	SH3PXD2A	4.93	PRIM2	4.77
FAM7A1	5.32	THC2770741	5.10	THC2640030	4.92	CHST15	4.77
PHLDB1	5.32	DSPP	5.09	ZNF835	4.92	STBD1	4.77
PTX3	5.31	AS3MT	5.09	TRIM66	4.92	WWC2	4.77
PLD1	5.31	ENST00000471093	5.08	RCAN3	4.92	BC035064	4.76
HIPK2	5.30	CENPF	5.07	SPC25	4.91	BQ064481	4.76
ARHGEF16	5.29	MCC	5.06	BRIP1	4.91	THC2553406	4.76
TP53I11	5.29	IFIT2	5.05	A_32_P80523	4.90	ANKRD36BP2	4.75
C2CD4C	5.29	KIAA0586	5.05	CASKIN2	4.89	POFUT1	4.75
FGFR1	5.29	SLC27A2	5.05	NBN	4.89	KIAA1211	4.75
C21orf58	5.28	MYEF2	5.04	THC2689241	4.89	C6orf170	4.75
STRN	5.27	BC032755	5.04	BMI1	4.89	DACT3	4.75
PARP4	5.26	RIMS3	5.04	TBC1D23	4.88	TTLL7	4.75
MDGA1	5.26	ROCK1	5.03	A_23_P96035	4.88	NHLRC2	4.74
KIAA0586	5.25	LOC100130428	5.01	GHR	4.87	MBOAT2	4.74
TDRD3	5.25	VMP1	5.00	DDX58	4.87	LGALSL	4.74
CENPK	5.25	AK096984	4.99	PARP11	4.87	UGP2	4.74
NAIP	5.24	KAT2B	4.99	A_24_P221285	4.87	DENND1B	4.73
TRIM43	5.24	C8orf83	4.99	PHF15	4.86	PPIG	4.73
CCDC40	5.22	A_32_P74901	4.99	ANKRD36B	4.85	KIF14	4.73
CETN3	5.20	NDRG1	4.98	LOC440288	4.84	CRY1	4.72

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
LOC653061	4.72	TBC1D8B	4.59	MYLK	4.47	PPP6C	4.40
GCLC	4.72	SDCCAG8	4.58	HSD17B11	4.47	CBX1	4.39
MNS1	4.72	ATXN3	4.58	C7orf13	4.47	LOC149351	4.39
MAGI1	4.72	HGF	4.58	FHL2	4.47	A_24_P106166	4.39
PIF1	4.71	A_24_P49657	4.57	WDFY2	4.47	DMRTC1	4.39
CRIP2	4.71	THC2740030	4.57	ZDHHC21	4.46	NFIL3	4.38
BC037919	4.71	A_24_P383598	4.56	CBX7	4.46	GNB5	4.38
HRK	4.71	TBC1D23	4.56	CREB1	4.46	C14orf28	4.37
ANKRD36B	4.71	TSPAN18	4.56	GRAMD1C	4.46	TYRP1	4.37
RHOU	4.71	ANO8	4.55	ASB5	4.45	FAM107B	4.37
FEZ1	4.71	ELK3	4.55	C6orf112	4.45	BRIP1	4.37
CPE	4.70	DAAM1	4.55	AZI1	4.45	DLGAP5	4.36
ANKRD36BP2	4.70	RAB33B	4.54	SLC30A6	4.45	SH3D21	4.36
ENST00000520259	4.70	CCDC82	4.54	LOC100506268	4.45	SMYD3	4.35
TMEM178	4.70	BC041996	4.54	ATP1A2	4.44	ENST00000485253	4.34
MYL3	4.69	IGFBP5	4.54	THC2519126	4.44	ANKRD36B	4.34
RNFT2	4.68	MIS18BP1	4.54	GAB1	4.44	FN1	4.34
LOC644246	4.68	KLHL5	4.54	ZBTB46	4.44	WNK4	4.34
THC2677286	4.68	CEP128	4.54	C16orf86	4.44	LOC84989	4.34
DKK3	4.67	CRYZ	4.53	C7orf74	4.44	WDR78	4.33
A1BG	4.67	ANKRD36	4.53	C9orf40	4.44	SH2B3	4.33
FERMT2	4.67	DAAM1	4.53	HS1BP3	4.44	PLAGL1	4.33
EPB41L1	4.65	IRX4	4.53	BC030094	4.43	ZNF618	4.33
CORO1A	4.64	SECTM1	4.52	PTPRH	4.43	DGKE	4.32
FGD3	4.64	ATP6V1E2	4.52	NUDT7	4.43	THC2616195	4.31
VCX2	4.64	DHFR	4.52	RAB30	4.43	KIAA1462	4.31
PHIP	4.64	NAIP	4.51	KLHL29	4.43	FAM155B	4.31
ESF1	4.63	C12orf48	4.51	ANGPTL2	4.42	MXI1	4.30
A_32_P138178	4.63	C18orf56	4.51	TIFA	4.42	LINC00421	4.30
BAI1	4.63	LRRFIP1	4.51	CABP1	4.42	TRPM7	4.30
BAIAP2L2	4.61	C20orf46	4.50	RNASEL	4.42	AMY1C	4.30
KCTD16	4.61	SCD5	4.50	RFFL	4.42	XM_929965	4.29
ENST00000446880	4.61	RIMKLB	4.50	ADAMTS1	4.42	SNX10	4.29
BBIP1	4.61	SGK1	4.49	C19orf57	4.41	A_24_P307384	4.29
LOC286382	4.60	TTC7A	4.49	EFNA2	4.41	DNAH10	4.28
A_32_P187518	4.60	RAB27A	4.49	CDC25C	4.41	RAB27A	4.28
IFT80	4.60	CA427179	4.48	AGAP7	4.41	DZIP1L	4.27
SKA1	4.60	ENST00000557373	4.48	PPM1L	4.40	AK128413	4.26
OSGIN2	4.59	CPEB1	4.48	RNFT1	4.40	ENST00000485364	4.25
CHMP4C	4.59	FAM161A	4.48	TBR1	4.40	C4orf46	4.25
		NARG2	4.47	SCAI	4.40		

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
HIPK2	4.25	EGR3	4.15	NES	4.03	LRRC32	3.96
APC2	4.25	SNHG10	4.14	MYT1	4.03	MORC2	3.96
LOC730101	4.24	ELL3	4.14	CDH23	4.03	THC2651023	3.96
BAIAP2	4.24	ENST00000456688	4.14	BC048213	4.03	FABP5	3.95
TOP2A	4.24	CD47	4.13	ZMAT1	4.03	A_32_P134556	3.95
RGS16	4.23	ZNF432	4.13	SCG5	4.03	C18orf1	3.95
RELL1	4.23	AGPAT4-IT1	4.13	AK054718	4.03	NDC80	3.94
SPEG	4.23	CENPI	4.13	SLC44A3	4.02	CCDC165	3.94
IL1RAP	4.21	BUB1	4.13	PLAUR	4.02	THC2536014	3.94
LOC727820	4.21	HERC4	4.13	LOC729732	4.02	NPL	3.94
RGPD5	4.20	MIS18BP1	4.13	PALM3	4.02	TRIB1	3.94
AIG1	4.20	WBP5	4.12	C8orf83	4.02	APOBEC3B	3.93
IVNS1ABP	4.20	A_32_P139311	4.12	DNMT3B	4.02	GBE1	3.93
KIF20B	4.20	RSU1	4.12	HDAC7	4.02	DOCK11	3.93
DNMT3A	4.20	ABCC2	4.12	PSTK	4.01	A_32_P215900	3.93
A_32_P65157	4.20	SGOL1	4.11	SPARC	4.01	GPR161	3.92
KIRREL2	4.19	RNFT2	4.11	BQ647583	4.01	TAGLN2	3.92
ENST00000538264	4.19	KLHL5	4.10	TRPM7	4.01	VASH2	3.92
ZFYVE28	4.19	MSI2	4.10	A_24_P910277	4.01	B3GNT2	3.92
ENST00000513644	4.19	ITGAV	4.09	ZNF197	4.01	SNX10	3.92
PAPPA	4.19	SLC30A3	4.08	AMOTL2	4.00	KHK	3.92
ASPM	4.18	KCNMB4	4.08	LOC100507507	4.00	LOC100652730	3.91
VLDLR	4.18	A_24_P161773	4.08	FANCD2	4.00	BC028022	3.91
AK075052	4.18	GCG	4.08	STYK1	4.00	JMJD1C	3.91
HPS1	4.18	RB1	4.07	A_24_P458252	4.00	C2orf63	3.90
SPATA17	4.18	TNIK	4.07	DKK1	3.99	AK098220	3.90
ZAR1	4.18	DECR1	4.07	C17orf100	3.98	CPPED1	3.90
GPC6	4.17	ANKRD36	4.07	FSTL5	3.98	TLN2	3.90
TRIM5	4.17	ANKRD42	4.07	EMP2	3.98	DEPDC4	3.89
FAM176B	4.17	ZRANB3	4.06	DSCC1	3.98	A_24_P272515	3.89
MFSD4	4.17	THC2756939	4.06	ENST00000535363	3.98	ATAD2	3.89
LOC100132057	4.16	A_24_P255123	4.06	KLF11	3.98	THC2691941	3.89
SLC9A6	4.16	THC2637568	4.06	CBX3P2	3.97	ZNF33A	3.89
GOLGA8E	4.16	AZI2	4.05	ROCK1P1	3.97	BRF1	3.89
VEGFC	4.16	DEPDC1B	4.05	THC2637707	3.97	KLHL5	3.89
VPS13B	4.16	AGPAT4	4.05	C10orf95	3.96	NEK2	3.88
ERN1	4.16	ROCK1	4.05	FAM101A	3.96	RAPH1	3.88
ANKRD42	4.16	JUN	4.05	ENST00000539568	3.96	ZNF273	3.88
G2E3	4.15	ZCCHC18	4.05	HRSP12	3.96	BDH2	3.88
DECR1	4.15	IL17RD	4.04	SRGAP2P1	3.96	WWOX	3.87
		CTNNB1	4.04			ENST00000545709	3.87

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
BMI1	3.87	WWTR1	3.79	AZI2	3.72	WWTR1	3.65
AK024566	3.87	TBXA2R	3.78	ARHGEF10	3.72	USP32P2	3.65
FAM100B	3.87	TC2N	3.78	LOC145783	3.71	HLA-DRB5	3.65
LOC729887	3.87	TCF4	3.78	LRRK1	3.71	BC004969	3.64
CGN	3.87	AF119908	3.78	PPFIA4	3.71	GCC2	3.64
THC2701403	3.86	A_24_P25040	3.78	ZNF423	3.71	TMOD3	3.64
CCDC148	3.86	BC007917	3.78	STAU2	3.71	RTN4RL2	3.64
GAB3	3.86	BX097783	3.77	CCDC88C	3.71	ABCC8	3.63
MYOM1	3.86	NUF2	3.77	SLC7A11	3.71	AHNAK	3.63
SLC39A8	3.86	PIGZ	3.77	THC2507829	3.71	ZDHHC15	3.63
CCL20	3.86	C1orf106	3.77	KREMEN2	3.71	C14orf109	3.63
SYTL2	3.86	MYCL1	3.77	NEK11	3.70	MAP6	3.63
RAPH1	3.86	ZCCHC24	3.77	THC2620541	3.70	A_24_P153234	3.63
TAF5	3.85	EPB41L1	3.77	PUS10	3.70	HSF2	3.62
TSPAN9	3.85	MBOAT2	3.77	CBX1	3.70	COTL1	3.62
VCAN	3.85	DPY19L2	3.77	RGS14	3.70	INPP5F	3.62
THC2496620	3.85	CAMK2G	3.76	A_32_P40673	3.69	SIPA1L2	3.62
WDR41	3.85	THC2655094	3.76	SGOL1	3.69	HIPK2	3.62
HEBP1	3.84	ZNF367	3.75	A_32_P21742	3.69	TCTN1	3.62
PFKFB4	3.84	FLNA	3.75	A_24_P383802	3.68	LRRC37A4	3.62
A_32_P181443	3.84	LOC100506123	3.75	PRMT2	3.68	BDNF	3.62
PLEKHA2	3.84	GEMIN8P4	3.75	CENPF	3.67	STK33	3.61
SWAP70	3.84	KLF11	3.75	CENPI	3.67	C17orf67	3.61
RAPGEF2	3.84	TGFBR2	3.75	CCDC88A	3.67	A_24_P930487	3.61
TNFAIP8L1	3.83	USP34	3.75	LRRC20	3.67	APAF1	3.60
MAPK11	3.83	PLK5	3.74	C8orf51	3.67	MMS19	3.60
PXN	3.83	VSIG10L	3.74	RCAN3	3.67	PPP1R21	3.60
NDNF	3.83	CPSF3	3.74	DPY19L4	3.67	BC005081	3.60
GPSM2	3.82	RP2	3.74	SAMD4A	3.67	TCF7	3.60
ARHGAP22	3.82	AW964144	3.74	ZNF613	3.67	SGMS2	3.60
CCDC88A	3.82	ADCY7	3.74	BPTF	3.66	LOC344595	3.59
ELOVL3	3.81	USP3	3.74	KIF15	3.66	HIPK2	3.59
JMJD1C	3.81	IL27RA	3.74	AATK	3.66	GALM	3.59
UNC5CL	3.81	EMP2	3.73	HIVEP3	3.66	C6orf170	3.59
A_32_P138666	3.81	GPR20	3.73	PARP11	3.66	PRCP	3.59
A_24_P733345	3.81	TTC33	3.73	AF339799	3.66	TRIM37	3.59
MMD	3.81	DOCK1	3.73	FEZ1	3.66	DUSP19	3.59
FMNL1	3.80	SMPX	3.73	FANCL	3.66	TBC1D1	3.59
THC2612011	3.80	LOC100507316	3.72	A_32_P205350	3.65	ACVR2B	3.59
SMA5	3.80	ARL15	3.72	A_24_P7565	3.65	DPF1	3.59
THC2558699	3.79	LMBRD2	3.72	TFDP2	3.65	A_23_P66347	3.58

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
UBR7	3.58	CAPRIN2	3.50	TCF15	3.44	CCDC109B	3.39
CBX1	3.58	AK123264	3.50	GMIP	3.44	SFR1	3.39
C21orf30	3.57	DLG3	3.50	KIAA1958	3.43	RELL2	3.38
DPY19L2P2	3.57	BMI1	3.49	SMCHD1	3.43	LSM3	3.38
HSF2	3.57	SEC61A2	3.49	TP53I3	3.43	BRCA1	3.38
PRAME	3.57	HTR7	3.49	ANKRD36	3.43	PGM2L1	3.38
DIP2A	3.57	A_23_P156609	3.49	RFFL	3.43	A_32_P57002	3.38
KIF20A	3.57	BC013798	3.49	PJA1	3.43	OBFC1	3.38
ELMO2	3.57	EIF2C4	3.49	A_24_P850336	3.43	THC2563460	3.38
ADAM17	3.57	ADAM19	3.48	LOC100506124	3.42	RPGR	3.37
ASPM	3.56	MCF2L	3.48	UCHL5	3.42	QKI	3.37
AK026418	3.56	A_24_P367169	3.48	VCX	3.42	DHRS2	3.37
EIF5A2	3.56	THC2643957	3.48	HDAC7	3.42	GALM	3.37
E01979	3.56	KIF16B	3.48	THC2543840	3.42	C18orf54	3.37
A_24_P126741	3.56	MAP3K14	3.48	MERTK	3.42	ENST00000446175	3.37
CCDC111	3.56	C1S	3.47	TDRD7	3.42	ARMCX3	3.37
ENST00000499653	3.55	C8orf59	3.47	PRKG1	3.42	ENST00000424852	3.36
HAUS4	3.55	CTAGE7P	3.47	CRADD	3.42	CDK19	3.36
SEC62	3.55	GYG2	3.46	ARL6IP5	3.41	SEPSECS	3.36
ARHGAP19	3.55	CCNB2	3.46	HCN3	3.41	TENC1	3.36
HEYL	3.55	RSAD2	3.46	CTDSPL	3.41	KLHL24	3.36
GPSM2	3.55	DKK3	3.46	NETO2	3.41	LOC728855	3.36
VASN	3.54	CMC1	3.46	LOC100506831	3.41	C12orf47	3.35
CUL5	3.54	ARMCX3	3.46	MORC2	3.41	LOH12CR2	3.35
ENST00000450308	3.53	KIF3C	3.46	SEL1L	3.41	PCDHB2	3.35
A_32_P182135	3.53	THC2677432	3.46	TANC2	3.41	MYLK	3.35
SLC39A4	3.53	NLGN4Y	3.46	HLA-DPB1	3.41	C9orf86	3.35
HS1BP3	3.52	GLRX	3.45	THC2648967	3.41	SLC2A14	3.34
LOC100133315	3.52	DLG5	3.45	TWSG1	3.41	FANCD2	3.34
GPR84	3.52	KATNAL1	3.45	PHF21B	3.40	AMOTL1	3.34
AZI2	3.52	AF339771	3.45	BBS9	3.40	SCAI	3.34
CARD8	3.51	ELL3	3.45	A_24_P701814	3.40	HECTD2	3.34
KIF18B	3.51	TTLL7	3.45	C2orf74	3.40	PDCL	3.34
ELK3	3.51	ENST00000421170	3.45	DENND1B	3.40	B3GNT1	3.34
CIT	3.50	TUBB2A	3.44	A_32_P112401	3.40	NBPF1	3.34
PUS10	3.50	CACNA1G	3.44	A_24_P41540	3.39	LOC390705	3.34
RASL11B	3.50	THC2586092	3.44	HIP1	3.39	A_24_P144254	3.34
SOSTDC1	3.50	KIRREL	3.44	MBNL2	3.39	DNAJC18	3.33
TMEM88	3.50	CCDC82	3.44	TMC7	3.39	C3orf18	3.33
RIMKLB	3.50	A_24_P273043	3.44	C10orf76	3.39	L3MBTL1	3.33
		A_24_P272653	3.44	CCDC88C	3.39		

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
TNFRSF25	3.33	TPM1	3.28	INPP5F	3.23	SATB2	3.18
KCNIP3	3.33	ZNF438	3.28	MTMR4	3.23	MYO5A	3.18
PTBP3	3.32	RNFT1	3.28	C10orf46	3.23	LOC100132790	3.18
TRPM3	3.32	CTAGE5	3.28	CNTRL	3.23	OSTF1	3.18
TMEM67	3.32	RAB3D	3.28	AJUBA	3.23	DEPDC1	3.18
AGBL2	3.32	C8orf37	3.27	VCX3A	3.22	THC2676635	3.18
C3orf64	3.32	C2orf48	3.27	ZNF780B	3.22	RNF43	3.17
C9orf93	3.32	C12orf48	3.27	PTGER2	3.22	DTNB	3.17
SPEF2	3.32	SMC2	3.27	THC2638238	3.22	ZBTB44	3.17
RSU1	3.32	INADL	3.27	LOC646719	3.22	INTS2	3.17
AZI1	3.32	ABCD4	3.27	GPD1L	3.21	PLD1	3.17
EPHB3	3.32	RADIL	3.27	LOC400027	3.21	C20orf201	3.16
C10orf58	3.32	SRBD1	3.27	PEX13	3.21	BTBD8	3.16
FAM76A	3.32	A_32_P70027	3.27	BC032907	3.21	APOBEC3F	3.16
ARL5B	3.32	PIAS4	3.27	RAD9B	3.21	LOC100132790	3.16
FAM59B	3.32	MYC	3.26	STBD1	3.21	TIA1	3.16
RAPGEF2	3.32	EXTL2	3.26	SPICE1	3.21	C14orf128	3.16
C14orf93	3.32	NUDT8	3.26	CDH24	3.21	ETV6	3.16
MYO5A	3.31	CASC5	3.26	HERC3	3.21	FGD3	3.15
IL28RA	3.31	SMC6	3.26	SENP7	3.20	BRCA2	3.15
SAMHD1	3.31	CLEC2D	3.26	HMGN5	3.20	XRN1	3.15
CHD6	3.31	PRPH2	3.26	A_24_P16291	3.20	TOR1AIP2	3.15
A_24_P84711	3.31	RNF213	3.26	LOC100506054	3.20	KIF18A	3.15
ENST00000414344	3.31	GPR107	3.26	NUDT14	3.20	U88048	3.14
PPP2R3A	3.31	RTKN2	3.26	COLEC11	3.20	MDM1	3.14
RHBDL3	3.31	POC1B	3.25	CEP68	3.20	STYX	3.14
RTN4RL1	3.31	JMJD1C	3.25	RHOQ	3.20	A_24_P170395	3.14
PVRL1	3.30	CDH23	3.25	COL6A1	3.20	PPP1R13L	3.14
OGG1	3.30	IKBKE	3.25	SLC7A10	3.20	A_24_P49860	3.14
ARHGEF19	3.30	MBTD1	3.25	SLC38A9	3.19	VAV2	3.14
GPR161	3.30	THC2666431	3.25	A_24_P229250	3.19	CPNE8	3.14
FAM82B	3.30	PCNT	3.25	ASAP3	3.19	BDP1	3.14
IL1R1	3.30	THC2700145	3.25	THC2481891	3.19	S1PR1	3.14
NLGN4X	3.30	KLHDC9	3.25	HTR7P1	3.19	KIAA1377	3.14
PDK2	3.30	ENST00000395427	3.24	BG695979	3.19	LOC100506268	3.14
MRPL35	3.29	DSCR9	3.24	PLEKHF2	3.19	ENST00000535261	3.14
NEK11	3.29	BC030106	3.24	GNPNAT1	3.19	ARRB1	3.14
KIF26A	3.29	TP73	3.24	FAM133A	3.18	FAM21C	3.14
CITED4	3.29	LOC100170939	3.24	ACOX1	3.18	FAM89A	3.14
NBN	3.28	A_24_P230009	3.23	PRKAR1A	3.18	MAPK8	3.13
BC014971	3.28	AFAP1	3.23	CALD1	3.18	WNT3	3.13

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
C2orf68	3.13	ANK2	3.08	SIPA1L3	3.04	SPAST	3.00
TIGD7	3.13	KIAA1841	3.08	ARHGEF40	3.04	ZFP37	3.00
RACGAP1	3.13	RBBP9	3.08	RECK	3.04	ENST00000440990	3.00
TLN2	3.13	C11orf41	3.08	ABCA10	3.04	BAG4	3.00
A_24_P101601	3.13	C16orf55	3.08	DDX26B	3.04	PDS5B	3.00
ALMS1	3.13	SGOL2	3.08	NYNRIN	3.03	AK023737	2.99
ENST00000459691	3.13	ZC3H15	3.08	UBE2D1	3.03	ENST00000514048	2.99
NIPSNAP3B	3.13	WDFY2	3.07	SUFU	3.03	AF222023	2.99
PBX1	3.13	TMEM187	3.07	LOC100288144	3.03	AK130207	2.99
A_24_P662366	3.13	ANKRD28	3.07	MPDZ	3.03	FAM21C	2.99
A_32_P180603	3.12	SKA2	3.07	SCN2B	3.02	U09850	2.99
LOC100289361	3.12	LYG1	3.07	USP18	3.02	GCC2	2.99
KIF1B	3.12	ZC4H2	3.07	PAIP2	3.02	THC2689749	2.99
RGPD2	3.12	NUB1	3.07	TTC25	3.02	ISG15	2.99
SS18L2	3.12	COMMD3	3.06	SOCS2	3.02	C5orf41	2.99
LOC100652973	3.12	MALT1	3.06	LSM14B	3.02	KIF1B	2.99
DUSP3	3.12	ESD	3.06	A_24_P289130	3.02	A_32_P13081	2.99
A_32_P223918	3.12	ALS2CR8	3.06	RNF217	3.02	RAB8B	2.98
C19orf51	3.12	LINC00115	3.06	TGFBI	3.02	AK054902	2.98
RGS14	3.12	CENPE	3.06	LOC100505679	3.02	SPPL2A	2.98
SLC27A1	3.11	DDAH2	3.06	PDLIM4	3.02	PSD3	2.98
FLJ42709	3.11	LGALSL	3.06	SMA4	3.01	TBC1D9	2.98
RBL1	3.11	EHD2	3.05	A_32_P142363	3.01	FZR1	2.98
RPH3AL	3.11	VPS53	3.05	ENST00000432751	3.01	GOLGA6C	2.98
MCM3AP-AS1	3.11	THC2650514	3.05	A_24_P631948	3.01	ARL10	2.98
ANKRD6	3.11	CR594811	3.05	RBKS	3.01	C2orf27A	2.98
CMIP	3.11	LRR1	3.05	C8orf37	3.01	SGPL1	2.98
IGFLR1	3.11	WDFY3-AS2	3.05	ESCO2	3.01	CORO2A	2.97
SRGAP3	3.10	ACOX1	3.05	RMI2	3.01	OBFC1	2.97
LOC100287628	3.10	PODXL2	3.05	ANKRD50	3.01	DYNC2H1	2.97
A_24_P246636	3.10	CXXC4	3.04	ARNTL2	3.01	RAPGEF6	2.97
FAM183B	3.10	BY796363	3.04	BC018626	3.01	A_24_P281468	2.97
CPNE3	3.10	IFIT5	3.04	FAM101A	3.01	EXOC6B	2.97
GDPD1	3.09	SEMA3G	3.04	BC004565	3.01	DICER1-AS	2.96
ENST00000424306	3.09	ACOT2	3.04	A_23_P14432	3.01	SNX5	2.96
THC2656116	3.09	ST3GAL5	3.04	SOX13	3.01	M14087	2.96
ZBTB44	3.09	ENST00000412019	3.04	ITPR1	3.00	A_24_P631625	2.96
CDH15	3.09	SH3KBP1	3.04	LRRN2	3.00	A_32_P36481	2.96
SOCS2	3.09	DOK4	3.04	THC2553512	3.00	NRBP2	2.96
NFAT5	3.08	RAI14	3.04	STK39	3.00	MYB	2.96
		DPY19L2	3.04	TSPAN14	3.00		

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation $\geq$2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
FAM184A	2.96	USP3	2.93	WDR48	2.89	FGFR1	2.86
PPP1R21	2.96	PDE7A	2.93	ATP8B5P	2.88	TIMELESS	2.86
ENST00000358073	2.96	TROVE2	2.92	PPAPDC3	2.88	MYO1B	2.86
GPR155	2.95	TOM1L1	2.92	HIST1H4L	2.88	BC033590	2.86
STK39	2.95	RAB6B	2.92	TTC30A	2.88	STRN	2.86
BC038432	2.95	A_32_P53558	2.92	HEATR5B	2.88	MEX3B	2.86
A_32_P38228	2.95	C21orf119	2.92	NSMCE4A	2.88	ADAM17	2.85
NBEAL1	2.95	CENPO	2.92	C1orf38	2.88	PDE4D	2.85
USP6	2.95	ZNF251	2.92	CCDC88B	2.88	TERF2	2.85
FAM21C	2.95	NUCB2	2.92	AF075008	2.88	TRIM23	2.85
A_24_P400751	2.95	GTF3C3	2.91	GBP5	2.88	LOC497257	2.85
TOM1L1	2.95	WDFY2	2.91	ZRANB3	2.88	FABP5	2.85
TNFAIP8L1	2.95	LOC286272	2.91	NIPSNAP3A	2.88	PPP2R5C	2.85
SERINC5	2.95	BICD1	2.91	MFAP3L	2.88	PNMA3	2.84
CTNNB1	2.95	ATP10D	2.91	C17orf51	2.88	PITPNC1	2.84
A_24_P92267	2.95	STK3	2.91	THC2633747	2.88	AHSA2	2.84
MAGEL2	2.95	KLHDC2	2.91	C5orf13	2.88	SCN5A	2.84
ENST00000415104	2.94	MCU	2.91	PPM1F	2.88	NETO2	2.84
ZHX1	2.94	PSIP1	2.91	HDX	2.88	TMEM123	2.84
DNAJC18	2.94	SH3PXD2B	2.91	LINC00087	2.88	HHEX	2.84
FABP5	2.94	FAM183A	2.90	CSTA	2.88	ENST00000261752	2.84
A_32_P42895	2.94	SLC17A5	2.90	A_24_P127425	2.87	ST6GAL1	2.84
SGMS1	2.94	CREBZF	2.90	RAB15	2.87	SCARF2	2.84
C21orf96	2.94	LACTB	2.90	NDC80	2.87	EDEM1	2.84
THC2670421	2.94	A2LD1	2.90	EIF4EBP2	2.87	UHRF1	2.84
GNG12	2.94	THC2756581	2.90	ITGB1BP1	2.87	OSR2	2.84
AA534873	2.94	FAM76A	2.90	MTDH	2.87	TSPAN13	2.84
CTNNB1	2.93	DFNA5	2.90	SPRYD7	2.87	C17orf108	2.83
DARS2	2.93	CABYR	2.90	DLG5	2.87	A_32_P152696	2.83
CTDSPL	2.93	HK1	2.90	ENST00000413722	2.87	FAM21C	2.83
SYT3	2.93	PLK4	2.89	SLC6A12	2.87	SLC7A11	2.83
CPNE8	2.93	MOB3B	2.89	KRTCAP3	2.87	HIST1H4B	2.83
BEND7	2.93	MPP3	2.89	FLYWCH2	2.87	SASH1	2.83
CCDC88A	2.93	LAMP3	2.89	VPS13C	2.86	USP6	2.83
NPHP4	2.93	TADA3	2.89	A_23_P99731	2.86	CCDC112	2.83
C3orf80	2.93	LOC100506965	2.89	GPR180	2.86	WHSC1	2.83
W22487	2.93	AK000053	2.89	AMDHD1	2.86	PDCD6IP	2.83
C1D	2.93	HPCAL4	2.89	SLC16A5	2.86	SH3BP5	2.83
RAB7L1	2.93	OSBPL5	2.89	UCHL1	2.86	AK098629	2.83
CAND1	2.93	GAS8	2.89	RAB8B	2.86	FHOD1	2.83
		TBC1D5	2.89	ARHGAP44	2.86	AK075186	2.83

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
USP32P1	2.83	SPOP	2.80	A_24_P350017	2.77	A_24_P341106	2.74
HIST1H2AL	2.83	A_24_P934939	2.80	AF100640	2.77	HYAL3	2.74
MYO19	2.82	ACOT7	2.80	MSN	2.77	LINC00085	2.74
SLC25A21	2.82	ABCC6	2.80	HIST1H4D	2.77	KIAA1109	2.73
MICU1	2.82	KLHL18	2.80	GNB4	2.76	RRM2	2.73
NEK2	2.82	CCNG2	2.80	EFNA4	2.76	LOC387723	2.73
PCYOX1	2.82	PRIMA1	2.79	PI4K2B	2.76	PBK	2.73
LOC344967	2.82	NAP1L1	2.79	BTN2A2	2.76	A_24_P925222	2.73
MPP3	2.82	MAGEA12	2.79	ZFP36L1	2.76	ARL17A	2.73
STT3B	2.82	FHL1	2.79	THC2736130	2.76	UBR1	2.73
ZFHX2	2.82	TPM1	2.79	EPB41L4B	2.76	SFRP4	2.73
GADD45B	2.81	RAB3D	2.79	A_24_P238836	2.76	GPR137C	2.73
ZNF850	2.81	IPMK	2.79	SRR	2.76	COX11	2.72
GNB4	2.81	EEF1A2	2.79	ZMIZ1	2.76	C1QL1	2.72
HIST1H4C	2.81	ZDHHC6	2.78	UBXN2A	2.76	BAG3	2.72
CU692129	2.81	CDC6	2.78	DENND4A	2.76	ZMAT1	2.72
LSM3	2.81	CU690915	2.78	THC2753400	2.76	ALG13	2.72
ACVR2B	2.81	A_24_P307395	2.78	BDP1	2.76	VPS29	2.72
FBLN5	2.81	CAMK1	2.78	IMPA1	2.76	ARMC9	2.72
ZDHHC21	2.81	DDX46	2.78	BDP1	2.76	KDM4D	2.72
FAM117A	2.81	FANCI	2.78	SOCS5	2.76	DENND5B	2.72
LEMD3	2.81	FSD1	2.78	A_32_P131583	2.75	BC066989	2.72
A_23_P115902	2.81	A_24_P144487	2.78	A_24_P58759	2.75	STARD5	2.72
ENST00000467537	2.81	PBX4	2.78	CAMK2G	2.75	ANKRD50	2.72
ZNF618	2.81	WLS	2.78	PELI1	2.75	CCDC88A	2.72
TOR1AIP2	2.81	RAD54B	2.78	ZRANB3	2.75	FAM47E	2.72
A_24_P560332	2.81	BG612665	2.78	ATP2B4	2.75	POLE2	2.72
LOC100505616	2.81	GUSBP3	2.78	SUMO3	2.75	STK38L	2.71
FUT8	2.80	LAG3	2.77	CASP6	2.75	TOM1L1	2.71
LUC7L3	2.80	NAGS	2.77	A_24_P152566	2.75	A_32_P57775	2.71
ENST00000451472	2.80	CEP128	2.77	AKAP5	2.75	THC2638025	2.71
ST13	2.80	KIAA1609	2.77	KLF10	2.75	TGIF1	2.71
MAP7D2	2.80	MNAT1	2.77	ZFAND4	2.75	SNN	2.71
SETDB2	2.80	TMEM19	2.77	XPNPEP3	2.75	SPATA6	2.71
GAB1	2.80	A_24_P911648	2.77	ENST00000528268	2.75	KDM3A	2.71
DYNC2H1	2.80	CLDN16	2.77	KIFAP3	2.75	SLC4A7	2.71
TUBA4A	2.80	BMPR2	2.77	A_32_P219377	2.74	IFT81	2.71
BIRC2	2.80	BM552308	2.77	SKA2	2.74	THC2674915	2.71
CHRNB1	2.80	SEC14L1	2.77	C21orf91	2.74	MSH2	2.70
KIAA1704	2.80	MICAL2	2.77	A_24_P25063	2.74	GPRASP1	2.70
		EFCAB11	2.77	DENND2C	2.74	BHLHB9	2.70

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SH2D4A	2.70	RAD18	2.67	ADD3	2.65	SAMD8	2.63
MYO15B	2.70	CENPP	2.67	HEXDC	2.65	AB593167	2.63
LPIN1	2.70	THC2671532	2.67	AHNAK	2.65	SPATA6	2.63
CEP78	2.70	UAP1L1	2.67	C2orf68	2.65	ENST00000539135	2.63
H2AFY2	2.70	THC2666580	2.67	STAT6	2.65	MEX3B	2.63
TUBA1C	2.70	CCNYL1	2.67	NAB1	2.65	A1BG	2.63
TTC7B	2.70	BG327427	2.66	PGM2	2.65	GPX8	2.63
A_24_P144337	2.70	SWAP70	2.66	C12orf47	2.65	ARL5B	2.62
DIP2B	2.70	LINC00312	2.66	FAM20C	2.65	PAWR	2.62
FAM175A	2.70	A_24_P916299	2.66	C14orf33	2.64	PPP2R2D	2.62
CHM	2.70	ERO1LB	2.66	SENP7	2.64	NEDD1	2.62
MRI1	2.70	SLC7A11	2.66	PEX2	2.64	UBTD1	2.62
MAFF	2.70	STYX	2.66	XPNPEP3	2.64	TRAF7	2.62
ARHGEF10L	2.69	SMURF2	2.66	NEK3	2.64	RGL3	2.62
U2AF1	2.69	C20orf96	2.66	C12orf75	2.64	P2RX7	2.62
UACA	2.69	SLC35G1	2.66	IKZF5	2.64	SNHG13	2.62
TCF15	2.69	A_32_P68205	2.66	ZNF876P	2.64	ITGB3BP	2.62
STK4	2.69	LOC344967	2.66	PLAT	2.64	DEPDC4	2.62
ROBO3	2.69	HDAC5	2.66	PRIM1	2.64	GLYATL1	2.62
A_32_P49164	2.69	S100A2	2.66	PTTG3P	2.64	IL1RAP	2.62
LOC728875	2.69	FBXW2	2.66	AL080082	2.64	EMILIN2	2.62
ENST00000523354	2.69	FRA10AC1	2.66	UPRT	2.64	A_32_P877	2.62
WDHD1	2.69	MYBL1	2.66	LOC254128	2.64	SMAGP	2.62
WDYHV1	2.69	A_32_P132169	2.66	CUTC	2.64	SERHL2	2.62
TBC1D19	2.69	DDX46	2.66	A_32_P22005	2.64	LOC100287525	2.62
FANCD2	2.68	A_32_P87849	2.66	MCEE	2.64	USP32	2.62
GJC3	2.68	GKAP1	2.66	SYNGR3	2.64	AL832582	2.62
GSTCD	2.68	DHFRL1	2.65	PDZD8	2.64	E2F8	2.62
CACYBP	2.68	WWP1	2.65	METTL15	2.64	ENST00000424349	2.62
HECTD2	2.68	A_23_P17152	2.65	GAGE7	2.64	BCCIP	2.61
A_24_P136155	2.68	TRPV4	2.65	ACOT11	2.64	ITPRIP	2.61
RPUSD3	2.68	AARSD1	2.65	KDM3A	2.63	C5orf30	2.61
KIAA0146	2.68	A_32_P220912	2.65	BG571904	2.63	ACVR2B	2.61
C5	2.68	FAM57B	2.65	MRPL43	2.63	PCDHB2	2.61
TRIM14	2.68	NEFL	2.65	SLC37A2	2.63	SYNE2	2.61
SPICE1	2.68	PKDCC	2.65	LANCL1	2.63	SLK	2.61
ZNF670	2.68	C2orf68	2.65	INCENP	2.63	A_24_P638453	2.61
AA968804	2.67	TBC1D12	2.65	RCBTB1	2.63	SUV39H2	2.61
AMT	2.67	DNAJC22	2.65	THC2632286	2.63	BMPR2	2.61
LINC00338	2.67	A_32_P7193	2.65	CMTM6	2.63	KDSR	2.61
SEC24A	2.67	IKZF5	2.65	DGKA	2.63		

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
MLF1IP	2.61	PPP2R3A	2.59	RALBP1	2.57	SYT15	2.54
C14orf142	2.61	IQCD	2.59	SEC61A2	2.57	XYLT2	2.54
UTP15	2.61	KLHL5	2.59	DYSF	2.57	NIN	2.54
NCAPD2	2.61	AL079294	2.59	C10orf57	2.56	FAM21A	2.54
THC2538610	2.61	B3GALTL	2.59	ANKRD58	2.56	CREB3L4	2.54
LRRC8B	2.61	MAPK8	2.59	GPR157	2.56	SIRT3	2.54
RAB43	2.61	H1F0	2.58	C15orf27	2.56	SH3KBP1	2.53
ATL3	2.61	PSTPIP2	2.58	C5orf56	2.56	LOC100507312	2.53
TNFSF4	2.60	ENST00000454471	2.58	SMAD3	2.56	TATDN1	2.53
FBXO33	2.60	DENND4A	2.58	FAM64A	2.56	RSU1	2.53
G2E3	2.60	RBBP5	2.58	OASL	2.56	ANTXR1	2.53
NSMCE4A	2.60	THC2541678	2.58	CREB3L2	2.56	L3MBTL1	2.53
AK074481	2.60	BC067908	2.58	RALGAPA2	2.56	SPRED2	2.53
GGH	2.60	ZBTB44	2.58	KIAA0196	2.56	GALNT4	2.53
ALAD	2.60	CXorf23	2.58	CYBRD1	2.56	A_32_P186678	2.53
VANGL1	2.60	THC2672768	2.58	BATF2	2.56	LOC100128822	2.53
THC2556546	2.60	KIAA0284	2.58	THC2628739	2.56	TMEM107	2.53
C12orf76	2.60	FSD1L	2.58	A_24_P392731	2.56	FZD5	2.53
ZCCHC11	2.60	KITLG	2.58	PDLIM2	2.55	MTAP	2.53
CK823339	2.60	A_24_P127042	2.58	PSME3	2.55	NRG2	2.53
LNPEP	2.60	KIF21A	2.58	KIAA0430	2.55	C17orf76	2.53
HOXC8	2.60	DAND5	2.58	C2orf56	2.55	ADK	2.53
A_24_P229728	2.60	GJC1	2.57	CHORDC1	2.55	C9orf140	2.52
AGAP7	2.60	ZNF71	2.57	SPAG9	2.55	C21orf91	2.52
AMDHD2	2.60	PPP1CB	2.57	A_23_P113263	2.55	A_24_P872359	2.52
EIF2C4	2.60	C1QTNF6	2.57	JAK1	2.55	A_24_P332461	2.52
NBR2	2.60	XRCC6BP1	2.57	SMYD2	2.55	CDKN2D	2.52
VTI1A	2.59	ICMT	2.57	ENST00000458030	2.55	THC2549822	2.52
RPL39L	2.59	RNF215	2.57	SRCIN1	2.55	LOC728705	2.52
CBX7	2.59	CKAP2L	2.57	RFC1	2.55	CDK2	2.52
CFLAR	2.59	TBC1D22A	2.57	BORA	2.55	ARNTL2	2.52
CACYBP	2.59	CEP152	2.57	IGSF3	2.54	A_24_P827794	2.52
A_32_P124833	2.59	EXTL1	2.57	TSPAN14	2.54	BUB3	2.52
C9orf30	2.59	BRWD1	2.57	TSPAN6	2.54	TTC32	2.52
USP12	2.59	C14orf49	2.57	ENST00000428309	2.54	CPNE3	2.52
CEP290	2.59	CD68	2.57	PNPLA6	2.54	SNX6	2.52
SIX3	2.59	ZCRB1	2.57	ENY2	2.54	PDCL	2.52
PARD3	2.59	EHBP1	2.57	A_32_P173955	2.54	INVS	2.52
SH2B3	2.59	GPRIN1	2.57	ZWINT	2.54	SPAG5	2.52
HDAC5	2.59	PPFIBP1	2.57	STMN1	2.54	CHMP3	2.52
HERC6	2.59	CAND2	2.57			DMC1	2.52

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
C5orf4	2.52	TMEM121	2.49	ZNF33A	2.47	CORT	2.46
NEIL3	2.52	CDC42EP3	2.49	PLCD3	2.47	ICT1	2.46
KCNN1	2.52	LOC100130171	2.49	TSEN54	2.47	RB1	2.46
HSD17B1	2.51	WDR92	2.49	GNPNAT1	2.47	BEND7	2.46
CENPC1	2.51	ARHGAP11A	2.49	UBE2C	2.47	THAP10	2.46
SFXN1	2.51	FZD2	2.49	PSTPIP2	2.47	GNB4	2.46
THC2746807	2.51	LANCL1	2.49	SPECC1	2.47	FAM200B	2.45
DEPDC7	2.51	ZC3H8	2.49	SMURF2	2.47	LINC00085	2.45
TMEM123	2.51	PIK3CA	2.49	DOCK7	2.47	MT2A	2.45
BIRC3	2.51	PPP2R1B	2.49	KLF13	2.47	A_24_P845631	2.45
SKA1	2.51	TMEM107	2.49	CARD8	2.47	A_24_P75558	2.45
MIS18A	2.51	AK095167	2.49	A_24_P670147	2.47	DLG3	2.45
A_24_P349539	2.51	IFT172	2.49	PRPS2	2.47	TCP11L1	2.45
TPRKB	2.50	WBP4	2.49	PPP1CB	2.47	LOC494150	2.45
TMEM180	2.50	SH3PXD2A	2.48	A_32_P156746	2.47	ABI2	2.45
ENST00000513071	2.50	MPST	2.48	ZAK	2.47	FARP1	2.45
TANK	2.50	UBR5	2.48	SCAMP5	2.47	RIN1	2.45
RNF213	2.50	SCARA3	2.48	CCDC151	2.47	MPDZ	2.44
HMGB3P1	2.50	AL049260	2.48	ENST00000535882	2.47	RAB3IP	2.44
CAMKMT	2.50	ARL6IP5	2.48	IFIT5	2.47	LOC100289230	2.44
COMTD1	2.50	CRYZL1	2.48	DMC1	2.47	NCS1	2.44
CENPJ	2.50	PDCD6IP	2.48	SUDS3	2.47	CNP	2.44
SLC44A1	2.50	C11orf71	2.48	ZNF251	2.47	HRC	2.44
C15orf41	2.50	HSPA12A	2.48	YBEY	2.46	A_24_P67063	2.44
A_24_P289043	2.50	LSM3	2.48	ESPL1	2.46	SCRN3	2.44
RNF19A	2.50	FAM114A1	2.48	GRTP1	2.46	LOC349196	2.44
SLC29A3	2.50	RNF214	2.48	VEZF1	2.46	CAPRIN2	2.44
CXXC4	2.50	THC2694186	2.48	CX783461	2.46	KLC1	2.44
NEDD1	2.50	NFU1	2.48	NHLRC2	2.46	NCAPG2	2.44
ARMCX2	2.50	MLL	2.48	POLE4	2.46	ROCK2	2.44
C4orf21	2.50	ZNF507	2.48	ANO6	2.46	HAUS3	2.44
IL27RA	2.49	BCL7C	2.48	SLC24A6	2.46	KIF11	2.44
CDC42EP4	2.49	FBXO33	2.48	ERBB2	2.46	ZNF618	2.44
MGC70870	2.49	CMTM6	2.48	PIGB	2.46	TSGA10	2.44
C8orf58	2.49	BC036625	2.48	NBPF11	2.46	OCLN	2.44
PNMA3	2.49	LSR	2.48	CCDC15	2.46	EPB41L5	2.44
CR599799	2.49	FAM164A	2.48	RGPD5	2.46	TRAF5	2.44
LINC00339	2.49	PARP2	2.48	A_24_P221485	2.46	DCLRE1A	2.44
LOC100134091	2.49	KNTC1	2.48	LCORL	2.46	DOK4	2.44
DUSP3	2.49	IQCG	2.48	FGFBP3	2.46	HDAC5	2.44
SMPDL3A	2.49	DNM1P46	2.48	ASAP2	2.46	YPEL5	2.43

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
A_32_P34372	2.43	CERK	2.41	THC2741040	2.39	STRBP	2.37
TMEM55A	2.43	PLSCR1	2.41	PIGK	2.39	PRMT2	2.37
GOLGA2	2.43	FAM115A	2.41	VSIG10L	2.39	MXD1	2.37
A_23_P125016	2.43	TBL1XR1	2.41	SHROOM1	2.39	MESDC1	2.37
MYO18A	2.43	PGPEP1	2.41	ALS2CL	2.39	POLA1	2.37
ZCWPW1	2.43	FANCG	2.41	NDRG4	2.39	LRRC40	2.37
NAGS	2.43	HNRNPL	2.41	CNOT6L	2.39	RNF2	2.37
INSIG2	2.43	CDCA4	2.41	PQLC3	2.39	LRRFIP2	2.37
ROM1	2.43	CDK1	2.41	KIAA1467	2.39	PDCD4	2.37
HGSNAT	2.43	LIMD2	2.41	SUMO3	2.39	ZDHHC15	2.36
JUP	2.43	PDE6D	2.41	C17orf53	2.39	THC2655194	2.36
GCC2	2.43	LPGAT1	2.41	FBXO4	2.39	TBC1D16	2.36
ASCC1	2.43	PPP2R5E	2.41	A_32_P212817	2.39	TMEM155	2.36
PPP6C	2.43	PPP6C	2.41	CLASP1	2.39	TCFL5	2.36
VEZF1	2.43	MTERFD1	2.41	C8orf44	2.39	MAPK10	2.36
NAB1	2.43	FAM111A	2.41	TP53TG3	2.39	FRA10AC1	2.36
ECT2	2.42	SESTD1	2.41	TDP1	2.39	CCDC136	2.36
JRKL	2.42	NSMCE2	2.41	MSL3P1	2.39	PRKD3	2.36
ACOT1	2.42	GPER	2.40	KCNH2	2.38	RGS12	2.36
DNASE1L1	2.42	UBA6	2.40	CKAP2	2.38	DYNC1LI1	2.36
LAPTM4A	2.42	TBC1D1	2.40	THC2672361	2.38	A_24_P324424	2.36
A_23_P113453	2.42	SKA2	2.40	TBC1D5	2.38	KIAA1841	2.36
LOC100131581	2.42	VPS13B	2.40	A_24_P315774	2.38	BBIP1	2.36
THC2564025	2.42	RNF213	2.40	ALMS1P	2.38	SNX33	2.36
CYB561	2.42	DYNC2LI1	2.40	RHOBTB3	2.38	STYX	2.36
SMURF1	2.42	CHMP3	2.40	CASP8	2.38	A_32_P46351	2.36
CACNB3	2.42	CCDC24	2.40	SSBP3	2.38	MFSD4	2.36
A_24_P324488	2.42	SEC22C	2.40	SLC2A3	2.38	A_32_P60687	2.36
PREPL	2.42	PARP11	2.40	FAM172A	2.38	ABCC5	2.36
HELZ	2.42	ICK	2.40	ZNF25	2.38	MDH1B	2.36
KLRG1	2.42	PIK3C2B	2.40	C2orf89	2.38	ZNF124	2.36
VRK2	2.42	UCHL5	2.40	SEC22C	2.37	C17orf53	2.36
HIP1	2.42	COTL1	2.40	KDM4C	2.37	BM687502	2.36
C15orf61	2.42	MIR210HG	2.40	A_32_P201792	2.37	STXBP4	2.36
F10	2.42	CTAGE5	2.40	NIN	2.37	CHMP5	2.36
TK1	2.41	CEP135	2.40	RMI1	2.37	XRCC1	2.36
RPL13P5	2.41	LLGL2	2.39	GFAP	2.37	GLT25D2	2.36
TTC7A	2.41	A_24_P306994	2.39	OBSL1	2.37	LOC100506922	2.36
USP9X	2.41	A_24_P24685	2.39	ENST00000375678	2.37	SPAST	2.36
CDC27	2.41	ANXA4	2.39	TPMT	2.37	A_32_P98854	2.36
CCDC125	2.41	ZNF642	2.39	C5orf62	2.37	NDRG3	2.35

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
OXTR	2.35	UBA6	2.34	FAM82B	2.32	MITD1	2.30
CPSF2	2.35	IDE	2.34	ZFAND6	2.32	DCUN1D1	2.30
C7orf55	2.35	STIL	2.33	C2CD3	2.32	LINC00265	2.30
PSRC1	2.35	PCSK7	2.33	RACGAP1	2.31	THC2786072	2.30
SMOX	2.35	RELL2	2.33	CDC45	2.31	A_32_P62480	2.30
FXR1	2.35	RALBP1	2.33	INPP4A	2.31	CDKN2C	2.30
HELLS	2.35	CAMK1D	2.33	ASXL2	2.31	ZBTB49	2.30
IL17RA	2.35	RNF157	2.33	ARNT	2.31	AHNAK	2.30
FANCI	2.35	AI791206	2.33	CWF19L1	2.31	COL18A1	2.30
NPHP1	2.35	WNK3	2.33	KIRREL	2.31	DHFR	2.30
GNAI3	2.35	A_32_P20717	2.33	FAM21A	2.31	SPTBN4	2.30
RGS10	2.35	PHTF1	2.33	APOOL	2.31	HSPB11	2.30
AI928490	2.35	SBF2	2.33	UGGT1	2.31	SMARCE1	2.30
MYSM1	2.35	L26245	2.33	LOC100507212	2.31	SNRPG	2.30
A_32_P201620	2.35	SIAH2	2.33	LOC644656	2.31	SMC4	2.30
FAM120C	2.35	A_24_P264004	2.33	RNF13	2.31	ZFYVE19	2.30
ENST00000492937	2.35	CTDSPL2	2.33	MPP1	2.31	A_24_P101541	2.29
LACTB2	2.35	PLEKHA1	2.33	FGD6	2.31	KIAA1143	2.29
RRM1	2.35	EPHB2	2.33	TARDBP	2.31	CLSPN	2.29
ATG4C	2.35	EP400	2.33	THC2683228	2.31	NFKB2	2.29
SLC6A13	2.35	INTS8	2.33	TERF1	2.31	A_24_P50328	2.29
ACTR2	2.34	THC2497722	2.33	LIX1L	2.31	TMEM194A	2.29
NUDT14	2.34	LOXL3	2.33	ABR	2.31	RDH10	2.29
RCCD1	2.34	NEFL	2.33	CLIP2	2.31	NUCKS1	2.29
PCMTD1	2.34	SOX4	2.33	TRIM44	2.31	DEPDC1	2.29
MKS1	2.34	PSD3	2.33	A_32_P154112	2.31	FAM49B	2.29
C9orf100	2.34	S100A10	2.32	GNB5	2.31	THC2619545	2.29
GRK5	2.34	FAM92A3	2.32	ENST00000428309	2.31	MAGED4B	2.29
RASL10A	2.34	NINL	2.32	A_32_P10100	2.31	BHLHE40	2.29
CRIPT	2.34	CRNKL1	2.32	C14orf118	2.31	C22orf36	2.29
TIA1	2.34	IGDCC4	2.32	XKR6	2.30	DZIP1	2.29
HMBOX1	2.34	SNAI2	2.32	TMEFF1	2.30	POLQ	2.29
A_32_P44916	2.34	C2CD3	2.32	DHFR	2.30	FGFR1	2.29
RAB43	2.34	THOC1	2.32	PHF21A	2.30	SRSF4	2.29
ARL6IP6	2.34	CCNYL1	2.32	MEX3A	2.30	GARNL3	2.29
SPCS3	2.34	CCDC89	2.32	ZNF711	2.30	RHOQ	2.29
CUBN	2.34	SRGAP2	2.32	A_24_P650562	2.30	CR604707	2.29
C1D	2.34	SHISA5	2.32	ABCB9	2.30	ENST00000556689	2.29
A_24_P33385	2.34	HPCA	2.32	A_23_P17444	2.30	CCDC150	2.29
A_24_P926993	2.34	ZBTB10	2.32	ITSN1	2.30	THC2525505	2.29
FEZ2	2.34	BDP1	2.32	EID2B	2.30	AK091492	2.28

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation $\geq$2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
MYCBP2	2.28	A_32_P36182	2.26	ANKRD57	2.25	EIF2AK3	2.23
MIPOL1	2.28	ANP32E	2.26	USP6NL	2.25	HLA-DQB1	2.23
ZNF652	2.28	DDX52	2.26	SASS6	2.25	A_24_P118391	2.23
AK022030	2.28	THC2517184	2.26	ENST00000429480	2.25	THC2683231	2.22
MORN4	2.28	CWC27	2.26	CLASP2	2.25	HTATSF1	2.22
RWDD3	2.28	C11orf30	2.26	CU676215	2.25	LOC728407	2.22
A_32_P44139	2.28	RASGEF1A	2.26	TNFAIP8L1	2.25	ENST00000424587	2.22
LOC389033	2.28	THC2676284	2.26	RFPL1-AS1	2.24	NBAS	2.22
CDC7	2.28	UBE2E2	2.26	NIN	2.24	A_24_P928489	2.22
GMFG	2.28	DISP2	2.26	LRP4	2.24	ATAD3B	2.22
MRE11A	2.28	EFNA1	2.26	MSI2	2.24	SAMD8	2.22
RHOF	2.28	STON1	2.26	MELK	2.24	KIAA1530	2.22
SPAG9	2.28	SEC14L1	2.26	THC2731337	2.24	MT2A	2.22
NEAT1	2.28	ZNF695	2.26	RNF130	2.24	TPM3	2.22
A_24_P33115	2.28	PLD2	2.26	ZNF853	2.24	C6orf145	2.22
PTTG1	2.28	GPRC5B	2.26	PBX1	2.24	ONECUT2	2.22
ERC1	2.28	PLEKHA8	2.26	TMC6	2.24	KIAA1279	2.22
AV753543	2.28	CKLF	2.26	A_24_P50639	2.24	SEPT7P2	2.22
RUFY2	2.28	RALB	2.26	DTNB	2.24	TIMELESS	2.22
CCNYL1	2.28	ACOT9	2.25	STRN3	2.24	NHLRC2	2.22
PTBP3	2.28	DUSP9	2.25	A_32_P16625	2.24	A_23_P51966	2.22
PKIB	2.28	PANX1	2.25	CDH10	2.24	SCAPER	2.22
RBM4B	2.28	CDKN3	2.25	NBR1	2.24	ADAMTS2	2.22
EHBP1L1	2.28	FBLIM1	2.25	GMPR2	2.24	FAM92A1	2.22
MTA3	2.27	DNAJC9	2.25	KIAA0101	2.24	KIAA1524	2.22
TTC15	2.27	SLC26A10	2.25	PLCD1	2.24	COX11	2.22
IL6R	2.27	NUDCD1	2.25	SRSF12	2.24	FAM123B	2.22
AK027667	2.27	A_24_P143653	2.25	AK123861	2.24	NKD2	2.22
WDR92	2.27	A_32_P48615	2.25	SYT15	2.23	C1orf187	2.22
A_24_P467805	2.27	DAZAP1	2.25	CLCN4	2.23	ADAM23	2.22
PSD3	2.27	CORO1C	2.25	OXNAD1	2.23	KIAA1143	2.22
MCF2L	2.27	A_24_P15803	2.25	LGALS1	2.23	FAM63A	2.22
LOC642852	2.27	C3orf23	2.25	DBF4B	2.23	MTCP1NB	2.22
FABP5	2.27	FBXL2	2.25	ACE	2.23	CPEB3	2.22
PCDH10	2.27	TRIM52	2.25	NLN	2.23	ZNF250	2.22
FNTA	2.27	ATG16L2	2.25	THC2746571	2.23	CEP290	2.22
QPCTL	2.27	THC2586905	2.25	PRKACB	2.23	RAD51C	2.21
DSCR3	2.26	AK091744	2.25	KIAA1109	2.23	PCYOX1	2.21
LRP12	2.26	NXT2	2.25	SMAD3	2.23	C18orf55	2.21
A_32_P2303	2.26	HNRNPL	2.25	NRTN	2.23	C14orf129	2.21
ENST00000512848	2.26	PIGC	2.25	LOC400043	2.23	ASGR1	2.21

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
C12orf53	2.21	DHX32	2.20	GPN3	2.18	MED12L	2.17
CCDC14	2.21	RALB	2.20	A_24_P340771	2.18	WHSC1	2.17
CAPRIN2	2.21	COPG2	2.20	XM_002343797	2.18	TYRO3	2.17
SENP2	2.21	THC2717907	2.20	OIP5	2.18	SAP30L	2.17
SLC25A12	2.21	PHIP	2.20	GPR180	2.18	TPM3	2.17
HAUS6	2.21	A_24_P790361	2.20	ENST00000426200	2.18	KIAA1958	2.17
DSCR3	2.21	U2SURP	2.20	WDHD1	2.18	ZNF548	2.17
CDC42	2.21	HERC1	2.19	A_24_P58034	2.18	PEX14	2.17
MSL3	2.21	EIF4EBP2	2.19	PLEKHM3	2.18	MRPL52	2.16
CNOT6L	2.21	RFXAP	2.19	CKB	2.18	LINC00471	2.16
SETD3	2.21	ARPC4-TTLL3	2.19	HNRNPA3	2.18	ECT2	2.16
GU228580	2.21	ROCK2	2.19	PRKAR1A	2.18	FRG1B	2.16
KDSR	2.21	MRPS16	2.19	LRRC4B	2.18	A_24_P204257	2.16
ALMS1	2.21	A_32_P121674	2.19	BC053353	2.18	GPR161	2.16
SIX2	2.21	ENST00000495461	2.19	ODF2L	2.18	NUDCD2	2.16
THC2603239	2.21	PCF11	2.19	GNPTAB	2.18	FAM172A	2.16
EFHD1	2.21	PDZD7	2.19	ADAM17	2.18	SLC44A1	2.16
ZRANB3	2.21	NRBP2	2.19	THC2598564	2.18	RHEBL1	2.16
SNAPC1	2.21	FMR1	2.19	LRRC37B	2.18	ACYP1	2.16
RAD51AP1	2.21	COTL1	2.19	RABGAP1L	2.18	LYRM7	2.16
RPL22L1	2.20	PFKP	2.19	SKIL	2.17	COX11	2.16
SMC4	2.20	DCTN2	2.19	THC2748306	2.17	YAP1	2.16
PRRG1	2.20	FAM82B	2.19	FOXRED2	2.17	DNA2	2.16
C18orf10	2.20	TRIM45	2.19	MIB1	2.17	NEK1	2.16
CEP57	2.20	CFD	2.19	MAP3K13	2.17	PHF15	2.16
SLC26A10	2.20	NKAPP1	2.19	KRAS	2.17	POLD3	2.16
CSNK1G3	2.20	CRABP2	2.19	NUPR1	2.17	FGD6	2.16
MEX3C	2.20	A_24_P366465	2.19	NP107054	2.17	WWTR1	2.16
STT3B	2.20	DEF6	2.19	MMS22L	2.17	SKA2	2.16
C12orf32	2.20	GEN1	2.19	TERF1	2.17	CCDC117	2.16
ABCA11P	2.20	SETD5	2.19	DOK3	2.17	RHOBTB2	2.16
MND1	2.20	ZFYVE1	2.19	RAB31	2.17	THC2505678	2.16
DIEXF	2.20	POLB	2.19	NT5DC1	2.17	PIF1	2.16
AK023629	2.20	LIMS1	2.19	UNC5B	2.17	CCDC150	2.16
THC2701748	2.20	ACTR2	2.19	PRL	2.17	PPFIBP1	2.15
VAT1	2.20	C4orf3	2.19	FAM72D	2.17	EG327585	2.15
ZNF726	2.20	XXYLT1	2.19	MALT1	2.17	B3GALTL	2.15
AZIN1	2.20	ZNF165	2.18	SEC31B	2.17	NCAPG	2.15
BC013423	2.20	EHBP1	2.18	EXOG	2.17	A_32_P53260	2.15
A_24_P530900	2.20	GMFB	2.18	A_32_P167592	2.17	ZFYVE20	2.15
FLVCR1-AS1	2.20	DMD	2.18	C17orf58	2.17	PLEKHO1	2.15

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ECD	2.15	A_23_P57836	2.13	SEC23A	2.12	CCNJ	2.11
BX094773	2.15	HSD17B7	2.13	CCDC75	2.12	CDON	2.11
NUDT6	2.15	NDRG2	2.13	KDM5A	2.12	NBL1	2.10
A_32_P176200	2.15	C14orf119	2.13	HOXC8	2.12	BM928667	2.10
TAGLN	2.15	FKBP5	2.13	FAM189B	2.12	BC084557	2.10
KLHL24	2.15	BRSK2	2.13	FAM96A	2.12	HIC1	2.10
SETDB2	2.15	CDK11B	2.13	RDH14	2.12	C12orf47	2.10
RBM4	2.14	PTTG2	2.13	VEGFB	2.12	EAPP	2.10
EXD2	2.14	C10orf140	2.13	A_24_P599225	2.12	MRPS25	2.10
EIF1B	2.14	LIMS3	2.13	XR_040656	2.12	SERINC2	2.10
A_24_P384200	2.14	AK3	2.13	HEATR5A	2.12	RAB33B	2.10
LOC645676	2.14	NANOS1	2.13	NFATC4	2.12	SUGT1	2.10
TADA3	2.14	UPRT	2.13	USP18	2.12	ENST00000443631	2.10
CUL4B	2.14	A_24_P922213	2.13	DNAH2	2.12	OST4	2.10
PGPEP1	2.14	CTAGE6P	2.13	LIF	2.12	YTHDC2	2.10
LOC100507303	2.14	CTAGE5	2.13	MIER1	2.12	SPACA4	2.10
CCNB1	2.14	GOLGA6L9	2.13	ZDHHC21	2.11	SAMD4A	2.10
CRYZL1	2.14	FLJ10038	2.13	FBXO41	2.11	RNMT	2.10
PABPC3	2.14	LRRFIP2	2.13	BAD	2.11	ACOT9	2.10
CCDC58	2.14	PACS1	2.13	RFC1	2.11	ZFYVE28	2.10
ARL5B	2.14	PPP2R5C	2.13	PFN4	2.11	C20orf108	2.10
ZNF821	2.14	ZNF395	2.13	MED30	2.11	THC2659348	2.10
HEG1	2.14	KREMEN1	2.13	DPH3P1	2.11	TFAM	2.10
GUSBP1	2.14	C11orf82	2.13	GHDC	2.11	PARG	2.10
LOC100507493	2.14	DYNLL2	2.13	ANKRD12	2.11	ZAK	2.10
OXCT1	2.14	A_32_P226751	2.12	A_24_P272352	2.11	B4GALT4	2.10
WDR66	2.14	A_32_P190097	2.12	GMCL1	2.11	TRIM62	2.10
A_24_P384411	2.14	ENST00000425338	2.12	ZFP36L1	2.11	THC2538534	2.10
YWHAQ	2.14	BM147583	2.12	PRMT2	2.11	EME1	2.10
THNSL2	2.14	SLC44A2	2.12	THC2633920	2.11	FAM83D	2.10
RASGRP2	2.14	CNOT10	2.12	FBF1	2.11	LRRC42	2.10
GFPT2	2.13	CEP68	2.12	A_24_P850187	2.11	KDM3A	2.10
AK027319	2.13	CDCA2	2.12	LOC441666	2.11	VPS29	2.10
KIF13B	2.13	MYL10	2.12	MLLT10	2.11	ZNF853	2.09
PGGT1B	2.13	ZDHHC20	2.12	WSB1	2.11	MGEA5	2.09
CEP152	2.13	PIBF1	2.12	TBCD	2.11	FGGY	2.09
PRKRA	2.13	TMPO	2.12	NEK3	2.11	ZFP30	2.09
IPO8	2.13	AK091057	2.12	MKI67	2.11	DNAJB5	2.09
LOC440104	2.13	NARF	2.12	REEP3	2.11	MEX3A	2.09
FLJ37453	2.13	A_24_P515815	2.12	TPM1	2.11	TAGLN2	2.09
ENST00000326237	2.13	CWF19L1	2.12	FOXM1	2.11	HPS4	2.09

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
GPR162	2.09	GPX8	2.08	GCFC1	2.07	PCMTD1	2.06
RUSC1	2.09	N4BP3	2.08	FAM101B	2.07	NMT1	2.06
PSPC1	2.09	CYB561	2.08	TTK	2.07	LSM11	2.06
GLIPR2	2.09	ATP11A	2.08	CU691169	2.07	TTC15	2.06
PEAK1	2.09	DOCK7	2.08	C19orf28	2.07	SLC41A1	2.05
ENST00000537659	2.09	RRP1B	2.08	STX2	2.07	IFNAR1	2.05
PPP1CB	2.09	C12orf32	2.08	TSSC1	2.07	TMEM126B	2.05
FAM165B	2.09	KRAS	2.08	TANK	2.07	TMEM52	2.05
KAZN	2.09	AK023038	2.08	PCGF3	2.07	CNTLN	2.05
C9orf103	2.09	PRPSAP1	2.08	UACA	2.07	ENST00000521696	2.05
RPP30	2.09	C20orf106	2.08	GOLGA8A	2.07	C10orf46	2.05
THC2672675	2.09	RUFY3	2.08	A_32_P190036	2.06	DZIP3	2.05
AK021443	2.09	MCM8	2.07	HSPBAP1	2.06	ANKRD13A	2.05
GHDC	2.09	GLRX3	2.07	AMT	2.06	ACTR1A	2.05
ANXA7	2.09	MYL12B	2.07	WDR19	2.06	KCNH3	2.05
SPC24	2.09	A_24_P878419	2.07	PCYOX1	2.06	C21orf90	2.05
CBX5	2.09	HELQ	2.07	VDR	2.06	BQ050540	2.05
LOC100240734	2.09	ZDHHC20	2.07	TXNRD3	2.06	DCK	2.05
POLE4	2.09	EXOC7	2.07	SPTY2D1	2.06	ARHGAP12	2.05
STC2	2.09	MAP3K5	2.07	NBPF15	2.06	GPX8	2.05
CANT1	2.09	FARP1	2.07	A_24_P882666	2.06	A_24_P127098	2.05
CYTH1	2.09	APPL2	2.07	CDS2	2.06	BIRC5	2.05
STRN3	2.09	EPB41	2.07	MDM4	2.06	TSPAN14	2.05
VAMP4	2.08	GSG1	2.07	LATS2	2.06	C22orf39	2.05
STRN3	2.08	COL9A3	2.07	FBXL15	2.06	A_24_P118382	2.05
HNRNPL	2.08	IFT80	2.07	YTHDC2	2.06	CTTNBP2NL	2.05
HIST1H2AB	2.08	THC2513403	2.07	PCDH10	2.06	NUDT12	2.05
KIAA0895L	2.08	CNP	2.07	CHM	2.06	CRBN	2.05
PLEKHG2	2.08	PARVG	2.07	KRT222	2.06	A_24_P367100	2.05
LOC100507599	2.08	HSP90AA1	2.07	NR2C1	2.06	GSTCD	2.05
HPCAL1	2.08	PPFIBP1	2.07	RHBDF1	2.06	RNF44	2.05
KATNAL1	2.08	THC2520108	2.07	A_32_P199725	2.06	RGS1	2.05
UHRF2	2.08	UEVLD	2.07	FGD6	2.06	SCLT1	2.05
LRRC37A2	2.08	TMEM48	2.07	VEGFB	2.06	H2AFJ	2.05
ADD3	2.08	TSNARE1	2.07	PSAT1	2.06	AFTPH	2.05
PPM1G	2.08	PLEKHA1	2.07	CCDC75	2.06	ARG2	2.05
FAM115A	2.08	SNRPD3	2.07	A_32_P16989	2.06	APBB1	2.05
RECQL	2.08	LOC389705	2.07	PCMTD2	2.06	FAM21C	2.05
THC2505678	2.08	ENY2	2.07	TIA1	2.06	ACADM	2.04
A_24_P712193	2.08	HIP1	2.07	ZFP90	2.06	LOC100505606	2.04
NFE2L3	2.08	RAB7L1	2.07	NTAN1	2.06	NLN	2.04

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
TTC35	2.04	ZBTB10	2.03	THC2555723	2.02	ST3GAL2	2.01
A_24_P67681	2.04	BLM	2.03	BAG4	2.02	DQ786199	2.01
HNRNPA3	2.04	CKS2	2.03	LIMK2	2.02	COX11	2.01
CCDC120	2.04	GOLGA8F	2.03	AGBL5	2.02	PJA2	2.01
OCLN	2.04	B3GNT5	2.03	CCDC112	2.02	BCL2A1	2.01
A_24_P281730	2.04	CENPJ	2.03	HAUS6	2.02	MBD2	2.01
SPTSSA	2.04	CNTROB	2.03	KIDINS220	2.02	OSBPL1A	2.01
ARMCX5	2.04	RBFOX2	2.03	CEP57L1	2.02	EHD4	2.01
AK090407	2.04	A_23_P4462	2.03	RB1CC1	2.02	SNPH	2.01
WWTR1	2.04	ATP6V1G1	2.03	THC2643296	2.02	LOC100131289	2.01
A_23_P151376	2.04	HADHB	2.03	PPID	2.02	PTER	2.01
ABCC5	2.04	CYBRD1	2.03	CCNE2	2.02	A_24_P143785	2.01
ARHGEF26	2.04	EVI5	2.03	ZRANB1	2.02	CSNK1G3	2.01
MAPKAPK3	2.04	ZNF518B	2.03	C17orf62	2.02	DUSP8	2.01
DNM3OS	2.04	ESCO1	2.03	MPP2	2.02	CORO6	2.01
NMB	2.04	DHFR	2.03	AF269286	2.02	FRYL	2.01
EFNB3	2.04	CNO	2.03	LRRC45	2.02	PLK1	2.01
GDPD5	2.04	SCN2B	2.03	ARHGAP19	2.01	A_32_P101844	2.01
SPRYD7	2.04	GTF3A	2.03	KIAA1704	2.01	NPRL3	2.01
COL1A2	2.04	PCGF3	2.03	TRUB1	2.01	EXOC1	2.01
EIF2C2	2.04	LOC645722	2.03	GOLGA6A	2.01	PNMA5	2.01
ARVCF	2.04	ENST00000423269	2.02	A_24_P7330	2.01	RAB5A	2.01
HOXC10	2.04	ANKRD20A9P	2.02	BU661610	2.01	SLC30A6	2.01
CLN3	2.04	A_23_P143676	2.02	RBM43	2.01	NUDT4	2.01
MDM1	2.04	KAZALD1	2.02	PCGF6	2.01	WDR11	2.01
MAP3K6	2.04	STXBP4	2.02	LRP12	2.01	C17orf39	2.00
A_24_P911327	2.03	LOC158960	2.02	RPS6KA3	2.01	THC2668815	2.00
INSR	2.03	CACYBP	2.02	ETNK2	2.01	ARHGAP11A	2.00
CGGBP1	2.03	A_24_P383934	2.02	ANKRD12	2.01	PHIP	2.00
JMY	2.03	CACNA2D2	2.02	C5orf44	2.01	GNA13	2.00
RPN1	2.03	NAT6	2.02	FAM110A	2.01	THC2683069	2.00
MRE11A	2.03	GEMIN2	2.02	CWF19L2	2.01	FAM108B1	2.00
UFL1	2.03	CTDSPL2	2.02	BE780682	2.01	PDE4DIP	2.00
RUNX3	2.03	MDH1	2.02	PHF7	2.01	ZNF207	2.00
LAMC3	2.03	ENST00000480427	2.02	S1PR2	2.01	MT2A	2.00
GOLGA8F	2.03	DCUN1D1	2.02	SEMA4F	2.01	IKZF4	2.00
ZNF280C	2.03	CYB561	2.02	BQ272125	2.01	THC2544355	2.00
BC034319	2.03	NEK3	2.02	OBSCN	2.01	SOAT1	2.00
RTEL1	2.03	THC2572360	2.02	ETHE1	2.01	ENST00000508688	2.00
GINS1	2.03	NCOR2	2.02	ENST00000376445	2.01	A_32_P96752	2.00
C15orf40	2.03			C1orf9	2.01	ARRB1	2.00

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ZWILCH	2.00	ZNF12	-2.02	A_24_P660797	-2.04	ZNF276	-2.06
ATP10A	-2.00	USP22	-2.02	MAB21L2	-2.04	MUL1	-2.06
PMS2L2	-2.00	A_24_P101771	-2.02	ZNF235	-2.04	PRR3	-2.06
PPPDE2	-2.00	SNX12	-2.02	CTU2	-2.04	ZDHHC5	-2.06
MRPL53	-2.00	GALNT11	-2.02	ISY1	-2.04	AGRN	-2.06
BAZ1B	-2.00	CCDC78	-2.02	PHKA1	-2.04	TBL2	-2.06
ODC1	-2.00	TOMM40	-2.02	FUT1	-2.04	ZNF44	-2.06
CPSF6	-2.00	PSEN2	-2.02	MKRN1	-2.04	A_24_P307368	-2.06
HLA-E	-2.00	DOM3Z	-2.02	ELOVL6	-2.05	MAP1LC3A	-2.07
THC2554943	-2.01	MSTO1	-2.03	ILF3	-2.05	ANKRD11	-2.07
A_24_P152793	-2.01	CASD1	-2.03	ST7	-2.05	FAM120B	-2.07
HLA-B	-2.01	SOD3	-2.03	GGTLC2	-2.05	LRP8	-2.07
CCDC48	-2.01	TSTD1	-2.03	PCCB	-2.05	FOXR1	-2.07
VTA1	-2.01	RNF216	-2.03	NSUN5P2	-2.05	THC2674530	-2.07
VPS26B	-2.01	ROPN1L	-2.03	PQLC2	-2.05	ING5	-2.07
IMP4	-2.01	MCAT	-2.03	RTTN	-2.05	FAM135A	-2.07
SH3BGRL2	-2.01	MBD3	-2.03	AKAP4	-2.05	SNRNP48	-2.07
A_32_P40667	-2.01	KCTD15	-2.03	TBRG4	-2.05	AI198876	-2.07
ZNRF1	-2.01	BNIP3	-2.03	FLJ45340	-2.05	RING1	-2.07
TRMT61A	-2.01	MAN2C1	-2.03	A_24_P859124	-2.05	C1QTNF4	-2.07
THC2559929	-2.01	BSG	-2.03	POMZP3	-2.05	A_32_P112034	-2.07
SLC22A18	-2.01	A_32_P133926	-2.03	RNPS1	-2.05	THC2634713	-2.07
MLH3	-2.01	GGT1	-2.03	BEND3	-2.05	B3GALNT2	-2.07
CCDC71	-2.02	CEP97	-2.03	THC2771474	-2.05	THC2505349	-2.07
CYP51A1	-2.02	ACAT2	-2.03	RPS10	-2.05	CEP41	-2.07
A_32_P107033	-2.02	A_23_P22086	-2.03	A_24_P24806	-2.05	TBC1D20	-2.07
RDBP	-2.02	LMTK2	-2.03	CXADRP3	-2.05	CD59	-2.07
TXNDC11	-2.02	TXNL4B	-2.03	A_24_P324644	-2.05	FJ159850	-2.07
CNOT4	-2.02	AGL	-2.03	MAN2B2	-2.05	KIAA0415	-2.07
ZNF462	-2.02	NDFIP1	-2.03	RHBDD3	-2.05	WRNIP1	-2.07
FUCA2	-2.02	PMS2	-2.03	C12orf5	-2.06	NDUFV3	-2.08
PDXK	-2.02	CLK4	-2.04	DPH2	-2.06	CYP51A1	-2.08
A_24_P298320	-2.02	THC2668244	-2.04	IMPAD1	-2.06	PILRA	-2.08
CUL7	-2.02	ENST00000404223	-2.04	BTBD9	-2.06	IVD	-2.08
ZDBF2	-2.02	PURA	-2.04	TOMM40	-2.06	DAP	-2.08
NOB1	-2.02	PARS2	-2.04	SPATA18	-2.06	ZNF202	-2.08
TRAF3IP1	-2.02	IFI27L1	-2.04	CCDC86	-2.06	MFGE8	-2.08
RAD23A	-2.02	LSG1	-2.04	A_24_P367259	-2.06	PPIA	-2.08
CA314185	-2.02	C6orf89	-2.04	ZNF512B	-2.06	THC2510958	-2.08
IRAK4	-2.02	A_24_P938006	-2.04	HDDC2	-2.06	TMEM30A	-2.08
A_23_P31563	-2.02	SURF6	-2.04	ENST00000355290	-2.06	ELOVL6	-2.08

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SPINT1	-2.08	DGKD	-2.11	SHC4	-2.13	LOC643401	-2.16
PAX4	-2.08	ATP5D	-2.11	LONRF1	-2.13	SOLH	-2.16
FLJ45340	-2.08	RBM38	-2.11	ZSCAN18	-2.13	NOXO1	-2.16
TNPO3	-2.08	GGT3P	-2.11	FLJ41350	-2.13	TRIM11	-2.16
LOC100133920	-2.08	IQCC	-2.11	STK25	-2.13	CCNC	-2.16
LYRM4	-2.09	CYCS	-2.11	CCDC132	-2.13	SND1	-2.16
AGRN	-2.09	ACAD8	-2.11	ATF5	-2.13	TRAF3IP1	-2.16
THC2677796	-2.09	SLMO2	-2.11	PDRG1	-2.13	ATAD3B	-2.16
PMS2L2	-2.09	POLD2	-2.11	LARP4B	-2.13	EPC1	-2.16
MRPL30	-2.09	ITPKC	-2.11	UBE3C	-2.13	APOBEC3F	-2.16
PRKAB1	-2.09	B4GALT5	-2.11	RASSF3	-2.14	SUMF2	-2.16
CAST	-2.09	ZKSCAN3	-2.11	HIST1H2BN	-2.14	PPM1E	-2.16
THC2623999	-2.09	UBAP2L	-2.11	MAFIP	-2.14	RABGAP1L	-2.16
ENST00000422603	-2.09	ARPC1A	-2.12	DTX3	-2.14	TXNDC11	-2.16
RHOBTB1	-2.09	RASA4	-2.12	ENST00000370708	-2.14	KBTBD4	-2.16
RCN1	-2.09	LOC92249	-2.12	SMARCD3	-2.14	SC5DL	-2.16
STK35	-2.09	KLHL21	-2.12	THC2721275	-2.14	GCC1	-2.16
ATP11C	-2.09	THC2730823	-2.12	CNN2	-2.14	KIAA0664	-2.17
TRMT61A	-2.09	PTPLAD1	-2.12	DDX39B	-2.14	DEGS1	-2.17
GRIN2C	-2.09	THC2671169	-2.12	EWSR1	-2.14	A_24_P401381	-2.17
PLAC8	-2.09	C6orf120	-2.12	HIST1H2BM	-2.14	A_24_P486503	-2.17
PPAN-P2RY11	-2.10	IFRD1	-2.12	PTCD1	-2.14	SMCR7L	-2.17
PYCR2	-2.10	GGT1	-2.12	PGAP3	-2.14	NFYA	-2.17
CDT1	-2.10	AK058117	-2.12	SHD	-2.14	PASK	-2.17
AGAP1	-2.10	ZNF511	-2.12	GRWD1	-2.14	C1orf109	-2.17
CHD7	-2.10	ACSS2	-2.12	NME9	-2.14	TLE3	-2.17
FLJ43663	-2.10	ALDH4A1	-2.12	CHMP2A	-2.14	ACADVL	-2.17
COPS8	-2.10	ZNF498	-2.12	A_24_P695691	-2.15	C14orf79	-2.17
ACTR5	-2.10	HIST1H2BE	-2.12	NDUFB4	-2.15	CA7	-2.17
SRM	-2.10	WBSCR22	-2.12	HSD11B1L	-2.15	WDR46	-2.18
VCP	-2.10	TTLL11	-2.12	FASTK	-2.15	RNASET2	-2.18
LRRC17	-2.10	ENST00000369381	-2.12	TRIM74	-2.15	DOLPP1	-2.18
EEF1D	-2.10	RIOK1	-2.12	HSPA6	-2.15	THC2687042	-2.18
OSBP	-2.10	CYCS	-2.12	ENST00000378337	-2.15	FLJ45340	-2.18
THC2612025	-2.10	FOS	-2.13	GPHA2	-2.15	C6orf204	-2.18
HSPB1	-2.10	INTS5	-2.13	CAST	-2.15	LOC100130557	-2.18
EPC1	-2.11	SESN2	-2.13	SLC25A26	-2.15	NIPSNAP1	-2.18
KIAA0240	-2.11	HIST1H2BO	-2.13	KDELR2	-2.15	THC2582296	-2.18
TP73-AS1	-2.11	ING5	-2.13	GANAB	-2.15	TXNDC5	-2.18
CREG1	-2.11	PILRB	-2.13	BMP7	-2.15	TM9SF4	-2.18
ALDH4A1	-2.11	RBM25	-2.13			PURB	-2.18

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
MST1P2	-2.18	MSLN	-2.21	DHX37	-2.24	CASD1	-2.27
NAT8L	-2.18	ZBTB7B	-2.21	ADAMTS3	-2.24	A_32_P106246	-2.27
NOP56	-2.18	FASTK	-2.21	COL3A1	-2.24	PHACTR3	-2.28
A_24_P725365	-2.18	TXNL4B	-2.21	THC2526647	-2.24	ZNF77	-2.28
ENST00000419956	-2.18	MSL1	-2.21	RNF146	-2.24	A_24_P323916	-2.28
STOML1	-2.18	C7orf26	-2.21	SMPD2	-2.24	C6orf89	-2.28
HCG18	-2.18	THAP4	-2.21	ENST00000509654	-2.24	RGS9	-2.28
CLCNKA	-2.18	WDR73	-2.22	PLCH1	-2.24	CDKN2A	-2.28
MST1	-2.18	PABPC4	-2.22	FXYD6	-2.24	SURF1	-2.28
RRP9	-2.18	ABCB10	-2.22	SRGN	-2.24	BCHE	-2.28
ZNF446	-2.19	SDCBP2	-2.22	POTEF	-2.24	THC2686110	-2.28
SLC2A9	-2.19	PCBD2	-2.22	THC2660636	-2.24	SHOX2	-2.28
CLCN3	-2.19	RABGAP1L	-2.22	THC2693923	-2.25	INO80	-2.28
C1orf114	-2.19	TNS3	-2.22	DNAJB9	-2.25	CXADR	-2.28
ZBTB9	-2.19	ATP8B3	-2.22	DLX5	-2.25	IP6K3	-2.29
CDKN2A	-2.19	CRYBA4	-2.22	AK025276	-2.25	FER1L4	-2.29
LONRF1	-2.19	DA093175	-2.22	THC2693741	-2.25	DRD5	-2.29
ATG4B	-2.19	THC2628527	-2.22	ALKBH4	-2.25	GADD45A	-2.29
LPCAT1	-2.19	A1CF	-2.22	CES2	-2.25	METTL1	-2.29
PPP2R2D	-2.19	EIF4H	-2.22	CUL1	-2.25	THC2540041	-2.29
B3GNT9	-2.19	DSE	-2.22	PHF23	-2.25	THC2694242	-2.29
RAB2A	-2.19	GTPBP6	-2.22	RABGAP1L	-2.26	PHKA1	-2.29
PRRC2A	-2.19	EMILIN3	-2.23	ACTR3B	-2.26	BAHD1	-2.29
ND1	-2.19	ZNF434	-2.23	MAGED1	-2.26	ATP5D	-2.29
YIPF6	-2.19	GGTLC2	-2.23	PRKAR1B	-2.26	GTPBP5	-2.29
A_24_P375435	-2.19	A_32_P178537	-2.23	AK055981	-2.26	GOSR1	-2.29
E2F4	-2.20	PPAN	-2.23	NDUFA10	-2.26	A_23_P119168	-2.29
PHF14	-2.20	BC009905	-2.23	AK026168	-2.26	FIS1	-2.29
RHBDD2	-2.20	SLC25A25	-2.23	GAS5	-2.26	SLITRK2	-2.30
KGFLP1	-2.20	CPSF6	-2.23	TMED9	-2.26	EMID1	-2.30
TPRN	-2.20	COL2A1	-2.23	A_24_P401521	-2.26	PIP5KL1	-2.30
X01147	-2.20	MMS22L	-2.23	ENST00000399269	-2.26	THC2680414	-2.30
QKI	-2.20	ZKSCAN1	-2.23	PRKRIP1	-2.26	CFLAR	-2.30
KDELR2	-2.20	EEF2	-2.23	LOC100287482	-2.26	TM7SF2	-2.30
A_32_P83221	-2.20	CUL1	-2.23	GTPBP5	-2.26	L3MBTL2	-2.30
UBE2L3	-2.21	OXR1	-2.23	DEGS1	-2.26	BCAS3	-2.30
STK19	-2.21	CDK13	-2.23	A_24_P370484	-2.27	ABCA7	-2.30
A_32_P100206	-2.21	ZNF3	-2.24	MGA	-2.27	ANKRD20A2	-2.30
HSPB1	-2.21	POLM	-2.24	SLC16A9	-2.27	ZNF12	-2.30
SCD	-2.21	A_24_P920715	-2.24	MAX	-2.27	AGK	-2.30
AKAP9	-2.21	PPP1R7	-2.24			ATP1B2	-2.30

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
THC2751913	-2.31	KGFLP2	-2.34	THC2610134	-2.38	SPDYE2	-2.43
A_23_P28397	-2.31	PURB	-2.34	RGL1	-2.38	ZFAND3	-2.43
ZNF764	-2.31	EME2	-2.34	A_24_P409471	-2.38	IMPDH1	-2.43
FTSJ2	-2.31	AHCY	-2.34	KIAA0090	-2.39	ENST00000443670	-2.43
ACTBL2	-2.31	HDAC4	-2.34	DDX56	-2.39	LRRC41	-2.43
BTNL2	-2.31	HFE	-2.35	POM121	-2.39	NOL6	-2.43
DPM3	-2.31	METTL1	-2.35	RNF145	-2.39	TYW1	-2.43
A_32_P149416	-2.31	POLH	-2.35	XPO5	-2.39	CTRL	-2.43
MAD2L1BP	-2.31	TMEM30A	-2.35	AES	-2.39	METTL7B	-2.44
THC2539541	-2.31	SAMD11	-2.35	TLCD1	-2.39	GNA11	-2.44
THC2551948	-2.31	ARID1A	-2.35	NUS1	-2.39	KIAA0930	-2.44
GGTLC1	-2.31	GSTT2	-2.35	ZC3HAV1	-2.40	C9orf167	-2.44
ST6GALNAC6	-2.31	DLEU2	-2.35	C6orf35	-2.40	LRPAP1	-2.44
ASCC3	-2.31	ABCA4	-2.35	MMAB	-2.40	ZBTB3	-2.44
RXRB	-2.31	NRXN1	-2.35	EIF4ENIF1	-2.40	A_32_P1841	-2.44
A_24_P549518	-2.31	DPM3	-2.35	GNA11	-2.40	SCFD2	-2.44
ZNHIT2	-2.32	GTPBP6	-2.35	IFRD1	-2.40	SLC2A1	-2.44
TNXB	-2.32	EIF3F	-2.35	BCR	-2.40	ASMTL-AS1	-2.45
AK021744	-2.32	ZNF394	-2.35	COG2	-2.40	TSPYL1	-2.45
AK7	-2.32	SOX1	-2.36	WDR25	-2.40	ATPBD4	-2.45
A_32_P139414	-2.32	HES2	-2.36	WTAP	-2.40	LOC100506687	-2.45
ABHD1	-2.32	FREM1	-2.36	RPF2	-2.41	CDT1	-2.45
GNL3L	-2.32	KDELR2	-2.36	FICD	-2.41	WBP1	-2.45
MTERFD2	-2.32	KLHDC10	-2.36	RBM4	-2.41	ESPNL	-2.45
DHCR24	-2.32	THC2704459	-2.36	ZC3H6	-2.41	THC2719547	-2.45
WDR1	-2.33	THC2534528	-2.36	TRAF3IP2	-2.41	CBX6	-2.45
THC2660977	-2.33	IMPDH1	-2.36	RABGEF1	-2.41	RIN2	-2.45
CCNO	-2.33	APOE	-2.36	LTBP2	-2.41	GMEB2	-2.45
HSPB1	-2.33	ENST00000434871	-2.36	SDSL	-2.41	RDM1	-2.45
YKT6	-2.33	BCL2L11	-2.36	SCHIP1	-2.41	AFG3L1P	-2.45
THC2718728	-2.33	A_24_P341489	-2.36	AGT	-2.42	YWHAG	-2.45
A_24_P108281	-2.33	NUS1	-2.37	ACAD10	-2.42	PSPH	-2.46
TCEAL7	-2.33	BRD2	-2.37	DDX17	-2.42	ANKRD11	-2.46
TRIM27	-2.33	PPM1J	-2.37	PRKAR2B	-2.42	MYO6	-2.46
PTPLAD1	-2.33	SPDYE3	-2.37	C6orf204	-2.42	PPP1R3F	-2.46
RBM15B	-2.33	FAM120C	-2.37	TAF8	-2.42	IL9R	-2.46
UTP14A	-2.33	HSPA8	-2.37	MICB	-2.42	SC5DL	-2.46
USP40	-2.34	ZNF397	-2.38	FIS1	-2.42	SULF2	-2.47
ZC3H10	-2.34	PDCD7	-2.38	USP14	-2.43	THC2787314	-2.47
OSBP	-2.34	SPATA2	-2.38	IGF2	-2.43	STRC	-2.47
CYP2A13	-2.34	SLC46A1	-2.38	THC2714457	-2.43	CD52	-2.47

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
LIPF	-2.47	COX19	-2.53	A_24_P170357	-2.58	RPL7L1	-2.65
A_32_P55438	-2.47	GCLM	-2.53	KDELR2	-2.58	PRDM13	-2.65
SLC2A13	-2.48	OGT	-2.53	FGF7	-2.59	WIPI2	-2.65
A_23_P71179	-2.48	TXLNA	-2.53	RBM14	-2.59	HFE	-2.65
MTG1	-2.48	SLC25A46	-2.53	RPL7L1	-2.59	WTAP	-2.65
ANKMY1	-2.48	COL3A1	-2.53	ZNF2	-2.59	FRMD4A	-2.66
BC043527	-2.48	A_24_P832737	-2.53	NIM1	-2.59	CDC42SE1	-2.66
NBEA	-2.48	PYGO1	-2.53	MYO6	-2.59	PPP1R1B	-2.66
HLA-B	-2.48	LRPAP1	-2.54	DNAH12	-2.60	ZNF498	-2.66
A_24_P505255	-2.48	ASCC3	-2.54	P2RY4	-2.60	ADAMTSL4	-2.66
A_32_P212654	-2.48	MTRF1L	-2.54	THC2663329	-2.60	LGI1	-2.66
GDF15	-2.48	ZNF433	-2.54	THC2610657	-2.60	LINC00301	-2.66
LOC283174	-2.49	POLR3H	-2.54	GNA12	-2.60	AK055679	-2.66
RCN1	-2.49	A_24_P516728	-2.54	PDCD7	-2.60	CHST2	-2.67
C20orf196	-2.49	CD164	-2.54	IRF5	-2.60	AKR1C3	-2.67
ACTR3B	-2.49	ZXDC	-2.55	PITRM1	-2.61	MLYCD	-2.67
AGAP3	-2.50	ANK3	-2.55	ND1	-2.61	KHDC1	-2.67
ADAMTS9-AS2	-2.50	CRYL1	-2.55	MTCH1	-2.61	RSPH1	-2.67
SLC46A1	-2.50	ZNF347	-2.55	EFCAB1	-2.61	CHD7	-2.67
ATG4B	-2.50	POM121	-2.55	COQ7	-2.61	UBAP1L	-2.67
ARMC5	-2.50	PURB	-2.55	THC2735727	-2.62	ZMAT3	-2.67
RTDR1	-2.50	RNPS1	-2.55	THC2544198	-2.62	GPATCH4	-2.67
AF116675	-2.51	LOC220906	-2.56	SYNM	-2.62	IDO2	-2.67
COG2	-2.51	EIF3B	-2.56	SLMO2	-2.62	THC2671553	-2.67
DQX1	-2.51	CD164	-2.56	LOC100133050	-2.62	HIST1H2BK	-2.68
THC2530905	-2.51	A_24_P478076	-2.56	KDELR2	-2.62	UBXN8	-2.68
MOP-1	-2.51	ING5	-2.56	SURF6	-2.62	CHGB	-2.68
A_24_P178167	-2.51	ZNF747	-2.56	DQ786230	-2.62	DDX19B	-2.68
LYRM4	-2.51	IRS1	-2.56	DRD5	-2.62	CBX6	-2.68
TBCC	-2.52	CHGB	-2.56	C12orf29	-2.62	GNAS	-2.68
COX6B2	-2.52	LTV1	-2.56	ACOT8	-2.62	ZNF800	-2.68
A_24_P392099	-2.52	REPS1	-2.56	GRIK5	-2.62	THSD4	-2.68
EIF3F	-2.52	A_23_P28927	-2.57	SLC39A7	-2.62	SLC35B2	-2.68
RASSF8	-2.52	CAPN10	-2.57	BX339010	-2.62	SARDH	-2.68
GET4	-2.52	ENST00000435913	-2.57	IMPDH1	-2.63	PMEL	-2.68
TAS2R14	-2.52	HIST1H2BH	-2.57	LARP1	-2.63	MTRF1L	-2.68
ENST00000521369	-2.52	A_24_P367249	-2.57	HIST1H2BL	-2.64	ZNF718	-2.68
LINC00328	-2.52	PTP4A1	-2.57	MYL4	-2.64	BRD2	-2.69
PLAC8	-2.53	ATRNL1	-2.57	PCCB	-2.64	CALN1	-2.69
APOBEC3C	-2.53	RABGAP1L	-2.57	ENST00000553155	-2.64	PEX6	-2.69
GBA2	-2.53	ZDHHC14	-2.58	EIF3F	-2.64	FAM3C	-2.69

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
C21orf81	-2.69	INSIG1	-2.76	PPIE	-2.84	A_32_P213389	-2.94
THC2648739	-2.70	A_32_P50508	-2.76	AKAP8L	-2.84	A_32_P145477	-2.96
UBR3	-2.70	BAX	-2.77	ZNF76	-2.84	ENST00000377186	-2.96
GNA12	-2.70	MGST2	-2.77	MIR7-3HG	-2.84	CLIP4	-2.96
MITF	-2.70	BC019703	-2.77	TFRC	-2.85	ILKAP	-2.97
AA837799	-2.70	BTG2	-2.77	A_24_P780609	-2.85	RRP7A	-2.97
C7orf50	-2.70	THC2616009	-2.78	CEP41	-2.85	POMZP3	-2.97
OSTM1	-2.70	RPS15A	-2.78	A_32_P192044	-2.85	A_32_P9532	-2.98
FAM3C	-2.71	A_32_P212764	-2.79	ASB1	-2.86	RASSF8	-2.98
A_32_P177595	-2.71	FLJ42627	-2.79	JAKMIP1	-2.87	SPAG4	-2.98
URGCP	-2.71	FCGBP	-2.79	RNASET2	-2.87	SMCR7L	-2.98
NPR1	-2.71	ABCF2	-2.79	EWSR1	-2.87	ANK3	-2.98
TXNRD1	-2.71	COL5A1	-2.79	SAA2	-2.88	WBSCR16	-2.98
KLK8	-2.71	CLYBL	-2.79	PDE1A	-2.88	DLX6	-2.98
FGF18	-2.71	THC2676741	-2.79	GLA	-2.89	MS4A5	-2.99
ACTN3	-2.71	MLLT4	-2.79	CNOT4	-2.89	MGC23270	-2.99
AK130366	-2.72	ADARB1	-2.79	METTL9	-2.89	PDK4	-2.99
HMOX1	-2.72	EIF4H	-2.80	ECHDC2	-2.89	LIFR	-2.99
TRPV2	-2.72	NDUFA10	-2.80	THC2685727	-2.90	LOC440356	-2.99
THC2562062	-2.72	POLR1C	-2.80	TMEM181	-2.90	KERA	-3.00
SLC12A2	-2.72	SETBP1	-2.80	FEM1A	-2.90	BC048283	-3.00
ZIC1	-2.72	ZNF689	-2.81	SLC12A2	-2.90	CEP97	-3.00
NSMAF	-2.73	MB	-2.81	NGFR	-2.90	ZNF79	-3.00
B4GALT1	-2.73	DMD	-2.81	AEN	-2.90	PMM2	-3.01
PTP4A1	-2.73	SRA1	-2.81	RAE1	-2.91	GPCPD1	-3.01
HSPA4	-2.73	NR5A1	-2.81	CDC42BPG	-2.91	THC2507435	-3.01
EXOC2	-2.73	FAM82A1	-2.81	LRRFIP1	-2.91	ZNF79	-3.02
AV756170	-2.73	SENP6	-2.81	PDCD2	-2.91	SLC35F2	-3.02
NDUFAF3	-2.73	MEG3	-2.81	HIST1H2BE	-2.91	TBRG4	-3.02
W27166	-2.73	NCDN	-2.81	POPDC3	-2.91	QPRT	-3.02
ABCF2	-2.74	ACTR3BP2	-2.81	NOXA1	-2.93	ERRFI1	-3.03
CD200	-2.74	U2AF2	-2.82	A_24_P916338	-2.93	BRF2	-3.03
NUP98	-2.74	PHF23	-2.82	LRRC47	-2.93	ENST00000426901	-3.03
THC2500237	-2.74	GNPDA1	-2.82	ATG16L1	-2.93	PRICKLE1	-3.03
CYP2E1	-2.75	KLRC1	-2.82	C9orf9	-2.93	FZD1	-3.03
CCNB2	-2.75	NCOA7	-2.82	MPV17L	-2.93	ENST00000435913	-3.03
HAPLN3	-2.75	ANK3	-2.82	EWSR1	-2.93	CRCP	-3.04
COL5A2	-2.75	DHCR7	-2.82	ING3	-2.94	A_24_P400645	-3.04
DHDH	-2.75	ZNF263	-2.82	EWSR1	-2.94	BX118285	-3.05
THC2540174	-2.75	ZSCAN21	-2.83	MTRF1L	-2.94	A_32_P101420	-3.06
A_24_P911306	-2.76	OLFM3	-2.83	SLC20A2	-2.94		

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
HIST1H2BF	-3.06	SAA1	-3.19	SCNN1A	-3.31	SNCA	-3.48
DNAH7	-3.06	PNMT	-3.19	SPATA18	-3.32	A_24_P871726	-3.48
LOC100131053	-3.06	SNCA	-3.19	FAM3C	-3.32	GLIS1	-3.49
C4orf34	-3.06	RAB36	-3.20	ZNF441	-3.32	MEGF8	-3.49
KANSL3	-3.06	SPRN	-3.22	BU903025	-3.33	C7orf58	-3.50
PLCH1	-3.07	ANKRD11	-3.22	BCKDHB	-3.33	ENST00000436263	-3.50
CATSPER3	-3.07	LOC729852	-3.22	CASP5	-3.34	C6orf204	-3.52
LOC388796	-3.07	CD24	-3.22	BG114486	-3.34	PCDHB5	-3.52
PTP4A1	-3.08	ANKRD20A5P	-3.22	MEGF11	-3.36	CXADR	-3.52
IDI2	-3.08	AK024956	-3.23	L07392	-3.36	FAM19A4	-3.53
HFE	-3.09	BC037328	-3.24	HDLBP	-3.37	FGF7	-3.54
METTL9	-3.09	SLC2A4	-3.24	RBAK-LOC389458	-3.37	AY227436	-3.54
ZP3	-3.10	STXBP5L	-3.25	AK092508	-3.37	A_32_P169383	-3.54
TNFRSF10B	-3.10	CBLN2	-3.25	ZEB2	-3.37	CD226	-3.56
ODZ3	-3.10	KBTBD3	-3.25	GNA12	-3.37	THC2677037	-3.56
SLC9A2	-3.10	DPYD	-3.26	FXYD2	-3.38	FOSL1	-3.57
ASMTL	-3.11	HTR3E	-3.26	CARKD	-3.38	SLC2A13	-3.58
A_32_P31827	-3.11	GTPBP4	-3.26	OR4X2	-3.38	CYCS	-3.59
USP7	-3.11	LHX2	-3.26	AK021570	-3.39	LOC339240	-3.61
A_32_P233727	-3.11	BU929651	-3.27	THC2652864	-3.39	SYCE3	-3.62
MEGF8	-3.11	ACSM3	-3.27	ING5	-3.39	LOC100506012	-3.62
COG2	-3.12	BCL7B	-3.27	FAM71E1	-3.39	PGAM2	-3.62
RUNX1T1	-3.12	NUS1	-3.27	CXCR7	-3.39	PCDH9	-3.63
QPRT	-3.12	B4GALT1	-3.28	CR749547	-3.39	SERPINB1	-3.63
FAM82A1	-3.13	DQX1	-3.28	AMBN	-3.40	ARID5B	-3.66
CLDND2	-3.14	PLEKHB1	-3.28	LOC439990	-3.40	RGS11	-3.67
LOC100507022	-3.14	DPYS	-3.28	ARID5B	-3.41	LOC100653030	-3.67
CCDC153	-3.14	PTGDS	-3.28	BCL11B	-3.41	SUV420H1	-3.67
PRKAR1B	-3.15	PELO	-3.28	PPP2R2B	-3.43	ASMTL	-3.67
TLE6	-3.15	OPTN	-3.29	ANKRD20A2	-3.43	A_32_P85230	-3.67
ICAM4	-3.15	FAM169A	-3.29	ODZ3	-3.44	CRCP	-3.67
SRXN1	-3.16	FAM169A	-3.29	AGTR1	-3.44	TMEM74	-3.68
ANXA11	-3.16	PKIG	-3.29	FGF18	-3.44	SCLY	-3.68
NOL6	-3.16	EPM2AIP1	-3.30	ENST00000456460	-3.44	COX10	-3.68
PTPRJ	-3.16	CRABP1	-3.30	LOC100133091	-3.45	ATP1B1	-3.69
METTL9	-3.17	GPR126	-3.30	THC2484716	-3.46	FAM120B	-3.69
THC2518214	-3.17	MDH2	-3.30	MAP2K6	-3.47	ABCA6	-3.70
MLIP	-3.18	HIST1H2BB	-3.30	DHCR24	-3.47	ITFG2	-3.70
FRRS1	-3.18	MAK	-3.30	OSGIN1	-3.47	SLC15A3	-3.71
SLC16A14	-3.18	THSD4	-3.31	ME1	-3.47	ZBTB24	-3.71
METTL16	-3.19	OBFC2A	-3.31			ZNF630	-3.72

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation $\geq$2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
DUSP23	-3.72	LOC157627	-3.91	LOC727916	-4.20	2	
PNMAL1	-3.74	KLHDC10	-3.92	RPL13	-4.21	EID3	-4.53
STAG3L4	-3.74	ENST00000553155	-3.93	LOC389834	-4.22	HUS1B	-4.54
FLRT3	-3.75	LOC642236	-3.95	DNAJC12	-4.25	ALDOC	-4.54
AI698357	-3.76	UTS2D	-3.96	LANCL2	-4.26	COLEC10	-4.56
LINC00256A	-3.76	FZD6	-3.96	NPFFR2	-4.26	VSTM2L	-4.56
AASS	-3.77	GLB1L2	-3.97	C9orf24	-4.26	NANOG	-4.58
BC062473	-3.77	ENST00000360902	-3.99	ENST00000415865	-4.27	AL834280	-4.61
KCND2	-3.77	GJC2	-3.99	CXADR	-4.27	TP53TG1	-4.62
PPM1E	-3.78	NKX2-1	-3.99	A_32_P150269	-4.27	THC2654921	-4.63
C7orf40	-3.78	HSD17B12	-4.00	USP40	-4.28	PPP1R3D	-4.64
BTBD9	-3.79	ARF1	-4.00	SLC22A18	-4.29	ENST00000503474	-4.65
ARF1	-3.79	C14orf81	-4.00	TLE1	-4.29	EFCAB1	-4.66
EPHA3	-3.79	RBM47	-4.00	THC2586657	-4.30	CU690253	-4.66
BF238843	-3.79	DNHD1	-4.01	THC2653997	-4.30	C1orf85	-4.70
TRAPPC6A	-3.79	ATP1B1	-4.01	CHPF2	-4.31	SOBP	-4.71
CYP2E1	-3.79	SDCBP	-4.02	ELOVL4	-4.31	BTG1	-4.71
RPL28	-3.80	CASP4	-4.03	AIFM2	-4.32	FAM59A	-4.73
A_32_P51313	-3.80	TAC3	-4.04	ACTG2	-4.32	BF207040	-4.73
NTRK3	-3.80	NLRP12	-4.04	PPP3CA	-4.32	AF119913	-4.73
A_23_P208582	-3.80	A_32_P99804	-4.05	ENST00000428471	-4.33	BC069749	-4.75
WNT5B	-3.81	NKX2-5	-4.09	RGMA	-4.35	LOC100505695	-4.76
FBXO27	-3.81	FOXD4	-4.10	NRXN1	-4.35	ZNF654	-4.76
KCNMA1	-3.81	SESN1	-4.11	MIOS	-4.37	KCNMA1	-4.78
MYPN	-3.81	LOC375295	-4.11	GNAS	-4.38	ENST00000519648	-4.78
PROM2	-3.82	AK127132	-4.12	DNALI1	-4.40	SESN1	-4.78
GRHL3	-3.83	CFI	-4.12	LOXL4	-4.41	THC2684874	-4.83
THC2679528	-3.83	DPPA2	-4.12	CASP4	-4.43	GNAS	-4.85
BRP44L	-3.84	MAGEC2	-4.12	TRIM4	-4.44	A_24_P917549	-4.86
LINC00478	-3.84	SOLH	-4.13	EPHA5	-4.45	ASPH	-4.87
ZDHHC8P1	-3.84	THC2679424	-4.14	IGFBP2	-4.46	LOC401431	-4.88
PCBD2	-3.85	DTX3	-4.16	MLLT3	-4.47	GLIPR1	-4.88
A_32_P41594	-3.85	CHPF2	-4.17	HSPA1A	-4.48	RPL27A	-4.88
GRK4	-3.86	RASSF8	-4.17	LOC100132167	-4.48	PELO	-4.88
C7orf50	-3.87	TXNIP	-4.17	ENST00000528660	-4.49	CYCS	-4.88
HOXD8	-3.87	SAT1	-4.19	PDE1A	-4.50	GLCCI1	-4.89
ST6GALNAC2	-3.88	LAMB1	-4.20	THC2754061	-4.51	CEP44	-4.89
SERPINB9	-3.89	CTH	-4.20	BEGAIN	-4.52	SLC43A2	-4.91
MGST1	-3.90	TMEFF2	-4.20	ASXL3	-4.53	ARHGAP4	-4.92
LOC151174	-3.90	INPP5D	-4.20	ENST00000538911	-4.53	SP5	-4.92
PPP1R3F	-3.91						

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
BCL2L11	-4.94	CALCA	-5.54	NEGR1	-6.20	SVOPL	-6.92
A_32_P38436	-4.95	AF074982	-5.56	CU675508	-6.21	LOC100506699	-6.95
CD247	-4.95	SPATA13	-5.59	GPCPD1	-6.21	C6orf35	-7.00
CD109	-4.96	PLCG2	-5.61	RIC3	-6.23	LRRK2	-7.04
A_32_P190334	-4.97	SPINK4	-5.62	PDE11A	-6.24	ABCA5	-7.09
ME1	-4.97	PRTFDC1	-5.63	CCDC3	-6.27	AK026195	-7.10
LBX1	-4.98	THC2685688	-5.64	PCDHB8	-6.28	ZNF831	-7.12
LIPG	-5.00	A_32_P179317	-5.65	A_32_P230537	-6.29	EFHC2	-7.15
A_32_P157471	-5.01	KIAA1217	-5.65	ANKRD20A2	-6.30	NPFFR2	-7.16
BC001335	-5.01	CNTNAP3	-5.66	EPHA7	-6.31	LOC100144602	-7.17
SNX7	-5.03	HTR1F	-5.68	TMEM26	-6.32	CNTN1	-7.18
SAT1	-5.03	FOSL1	-5.68	HLA-DMA	-6.33	RERG	-7.19
PALMD	-5.07	THC2679528	-5.68	PDZD2	-6.34	LOC100288911	-7.21
DKFZP564C152	-5.08	TLE2	-5.69	FAM74A1	-6.37	BF217859	-7.24
NPR2	-5.08	BC001335	-5.69	DMRTA1	-6.38	CASP10	-7.29
MSH3	-5.11	PDE11A	-5.71	TP53TG1	-6.38	AK026965	-7.33
THC2713242	-5.14	SGCG	-5.71	ABCA5	-6.39	BI836406	-7.37
SEMA6D	-5.14	A_32_P108277	-5.71	ANKMY1	-6.39	CHRNA3	-7.37
TCN2	-5.15	BX107298	-5.72	ACACA	-6.45	THC2624002	-7.38
PDE11A	-5.16	NFYA	-5.73	ME1	-6.45	HMCN1	-7.40
NR4A2	-5.17	WDR33	-5.78	FAS	-6.46	HES1	-7.41
ANKRD20A2	-5.20	CPXM1	-5.82	A_32_P35294	-6.46	PLCB1	-7.41
FBN2	-5.21	ARID5B	-5.82	GPC4	-6.49	KATNAL2	-7.42
RGS11	-5.25	SLC16A14	-5.83	ARHGAP9	-6.50	THC2661509	-7.43
C6orf48	-5.25	S100A6	-5.83	MYO3B	-6.53	NFIA	-7.44
DOCK8	-5.29	NPY1R	-5.92	SUSD1	-6.55	MSH3	-7.45
C20orf103	-5.33	PDE1A	-5.95	SFRP1	-6.56	A_32_P101860	-7.46
THC2699065	-5.35	SSPN	-6.01	CARD6	-6.58	CFH	-7.48
CRNDE	-5.38	LTK	-6.03	EFHC2	-6.58	THC2621221	-7.48
PLXNA1	-5.38	PTPRK	-6.04	DOK6	-6.60	THC2726661	-7.49
IFI27L2	-5.39	DCLK1	-6.05	CNTNAP3B	-6.65	A_32_P72541	-7.58
ZMYND12	-5.40	SLC3A1	-6.05	TLE6	-6.68	LINC00470	-7.60
FOXN4	-5.41	PNMAL1	-6.07	SP5	-6.68	PPP1R1C	-7.71
ENST00000520594	-5.42	RIMS2	-6.08	CASP10	-6.69	TNFRSF10D	-7.73
TMEM26	-5.42	AK001116	-6.12	THC2677659	-6.72	A_32_P306001	-7.76
HSD17B8	-5.46	FAM59A	-6.12	DOK6	-6.75	GCNT2	-7.81
CEP44	-5.47	SLC43A2	-6.13	PTGFRN	-6.76	IGF1R	-7.81
COL20A1	-5.48	DTX3	-6.15	SESN3	-6.79	SLC16A6	-7.92
CNTN1	-5.52	ENO2	-6.15	LAYN	-6.79	EIF3F	-7.92
KCTD1	-5.53	CR936711	-6.17	MIOS	-6.80	SEMA5A	-7.95
ANKRD20A2	-5.53	EPCAM	-6.18	PDLIM3	-6.87	LMO1	-7.96

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
FBP1	-7.98	SLC16A6	-9.66	RERG	-11.54	GCH1	-14.94
RSPO2	-8.01	PTN	-9.68	SLITRK6	-11.57	NPR3	-15.04
CFH	-8.07	AK027541	-9.72	QPCT	-11.68	PIK3C2G	-15.25
P2RX5	-8.12	NDUFA10	-9.74	BF217859	-11.70	ODZ3	-15.42
RASSF8	-8.13	PDE3A	-9.76	PITX1	-11.80	ELF4	-15.59
TBX18	-8.15	THC2664860	-9.78	A_32_P212958	-11.81	AGTR1	-15.74
LRRC70	-8.24	LHFP	-9.79	HECA	-11.90	SLC38A5	-15.84
MYLIP	-8.30	LINC00470	-9.84	ZFPM2	-12.07	TNFRSF11B	-15.94
LOC375295	-8.34	S100A11	-9.88	FBXO8	-12.24	BX538139	-16.03
A_32_P9737	-8.38	AK022020	-9.89	TPD52L1	-12.29	PRINS	-16.06
A_32_P222241	-8.39	ACSBG1	-9.89	KCTD1	-12.41	APOL6	-16.11
TSPAN8	-8.52	A_32_P192389	-9.99	CFH	-12.68	SLITRK3	-16.13
RSPO2	-8.53	KCNK12	-10.15	LDHD	-12.80	CHST9	-16.26
THC2496768	-8.61	A_32_P210193	-10.16	AGPHD1	-12.82	A_32_P137075	-16.29
IL3RA	-8.66	A_32_P121978	-10.20	CDKN1A	-12.93	CROT	-16.35
CA3	-8.67	ENST00000507916	-10.22	PDE6H	-12.97	DMRT3	-16.45
GLCCI1	-8.68	PPP4R4	-10.29	BM807051	-13.00	L1TD1	-16.60
RFPL1	-8.69	CDKN1A	-10.30	THC2765857	-13.09	KCNJ2	-16.78
A_23_P149270	-8.75	RIN2	-10.36	DLC1	-13.18	THC2644897	-16.80
MLLT3	-8.82	TDRD1	-10.37	MEST	-13.19	ADAMTS19	-16.81
BOC	-8.84	PDE1A	-10.39	ISOC1	-13.21	PTN	-16.91
TLX3	-8.92	LIPG	-10.43	HES1	-13.22	MAOB	-17.02
THC2512148	-8.93	HLA-DMA	-10.48	A_24_P910080	-13.35	CPA2	-17.17
MIR137HG	-8.94	CA8	-10.50	C8orf85	-13.42	THC2520542	-17.32
CDCA7L	-8.96	CNTNAP3	-10.50	LOC100505806	-13.45	MSX2P1	-17.61
ITGA2	-8.98	PALMD	-10.62	CTNNA3	-13.59	COCH	-17.73
IRX5	-9.00	CD109	-10.66	DNAH7	-13.62	MYO3B	-17.76
CU690251	-9.00	KBTBD10	-10.73	KCNQ2	-13.87	LOC90499	-17.80
C14orf23	-9.12	DMKN	-10.74	FAM198B	-13.88	THC2646628	-17.89
LOC284561	-9.12	ZMAT4	-10.74	DMD	-13.91	SEMA6A	-17.92
CARD18	-9.13	HUS1B	-10.75	PTPRJ	-13.91	LOC285141	-18.11
BAI3	-9.14	LMO4	-10.76	THC2696414	-13.94	ODZ3	-18.18
DNAH12	-9.30	MLKL	-10.88	NDUFA10	-14.22	FBLN2	-18.19
CNR1	-9.36	FUT4	-10.91	MAL2	-14.23	ALDH1L1	-18.47
DNAH11	-9.37	GSTO2	-10.94	SLC8A1	-14.40	PRDM1	-18.53
FGL1	-9.40	LOC100505938	-11.07	FAM74A3	-14.51	TNFSF10	-18.54
ARSI	-9.44	A_32_P128952	-11.26	AGPAT9	-14.57	TFPI	-18.65
CFHR3	-9.46	MYLIP	-11.26	BE672039	-14.61	BE904671	-18.68
SSPO	-9.54	DMRT1	-11.30	FAM111B	-14.68	CU675788	-18.85
PCDHB16	-9.58	CER1	-11.33	ALX1	-14.73	FOXG1	-18.86
ATP8B3	-9.61	NDST4	-11.51	TACSTD2	-14.84	GPM6B	-18.91

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
CNTNAP3B	-19.05	THC2535223	-29.52	LGALS3	-44.63	THC2730631	-87.70
CTSF	-19.65	S100A11	-29.61	RUNDC3B	-44.69	CBR3	-89.26
COCH	-19.77	SLITRK1	-29.78	DLC1	-45.44	IRX3	-91.59
BACH2	-19.81	PLAC1	-29.96	IGF1R	-45.75	PDZRN4	-91.71
ICA1	-19.99	TOX	-30.23	NTS	-45.82	HSD17B12	-91.87
GPC3	-20.06	CHODL	-30.23	CU675110	-46.71	SORBS2	-92.26
HYLS1	-20.12	TNFRSF11B	-30.85	NFIA	-47.00	GAD1	-92.87
HTATIP2	-20.12	SPP1	-31.12	DMRT3	-48.12	ZFPM2	-94.88
BMPER	-20.53	SCRG1	-31.27	BM989848	-48.41	MPPED2	-95.22
IDO1	-20.57	AW977527	-31.45	SFRP1	-50.55	ANKRD22	-95.24
A_32_P191141	-20.72	NFIA	-31.71	CDH2	-51.83	MMRN1	-95.87
LOC100132735	-21.07	SLC8A1	-31.95	CITED2	-54.75	TMEM26	-99.26
MEF2C	-21.24	ICA1	-32.02	C4orf49	-55.16	OTOA	-99.75
MSX2	-21.41	P2RX5	-32.03	GAD1	-55.30	BST2	-105.9
TLX1	-21.48	DNAJC15	-32.85	CAMK4	-55.50	KIAA1217	-113.8
THC2781239	-21.50	TOX	-33.05	ASB9	-56.89	LUM	-114.6
SLC30A8	-21.79	MLH1	-33.99	PEG10	-57.48	DCN	-126.6
THC2645398	-21.85	ACTA2	-34.25	AK094603	-59.54	SLITRK1	-131.2
A_24_P489649	-21.96	POU1F1	-34.27	CBR1	-59.90	ANXA1	-132.5
GCH1	-22.57	EPHX2	-34.80	ECEL1	-60.29	TMPRSS15	-136.5
RBM47	-22.97	C8orf4	-35.22	HAPLN1	-60.94	RASSF9	-141.9
NDP	-23.42	FBN2	-35.35	KLHL14	-61.18	METTL7A	-149.7
FOXG1	-23.70	EDIL3	-35.37	HTATIP2	-61.53	MAOB	-150.7
SEMA5A	-24.01	MYH11	-35.84	EFNB2	-63.44	SNTG1	-151.6
FAM5C	-24.13	LINGO2	-36.40	KANK1	-64.16	FBN2	-153.9
TRIM56	-24.15	RHOH	-37.02	ASXL3	-65.89	THC2682885	-155.6
PPP4R4	-24.28	METTL7A	-37.92	STXBP5L	-66.04	ALDH1A1	-156.1
RARB	-24.42	BHLHE41	-37.93	ERP27	-66.33	DCDC5	-161.2
SORBS2	-25.12	CNTNAP2	-38.40	PCDH9	-66.81	KANK1	-175.8
ZP3	-25.38	C18orf34	-39.28	SGCE	-67.77	STAMBPL1	-177.9
LUM	-25.58	CYB5A	-39.29	CGREF1	-74.70	CHRNA9	-202.3
MYH11	-25.61	RNLS	-39.40	QPCT	-75.40	ITGA1	-205.2
PDZRN4	-25.72	FAM46A	-39.66	C8orf4	-75.87	ARHGDIB	-215.1
THC2744399	-25.88	EPM2AIP1	-40.06	SLC13A3	-75.88	PCDH20	-215.6
HSD17B12	-26.44	LOC284244	-42.46	MDK	-76.22	LRP1B	-218.4
PAX6	-26.91	BAMBI	-42.80	KCNK10	-79.70	SLC27A6	-257.3
TMCO4	-27.07	EPHB6	-42.84	BEX2	-80.61	MPPED2	-262.7
ISL1	-27.39	MLKL	-43.20	BAALC	-81.03	HAND2	-267.0
TFPI	-27.94	RERGL	-43.66	SLC8A1	-81.54	TSLP	-421.4
SEMA6A	-28.84	XIRP2	-43.75	MGAT4C	-81.61	DLC1	-424.0
THC2712710	-29.29	SPOCK3	-44.18	BEX1	-81.81	VGLL3	-466.6

Appendix III Gene Expression Changes in $A2780_{CBN\text{-}DXL}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation $\geq$2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ABCB1	-559.8						
CYB5R2	-657.1						
DLK1	-927.8						
ENST00000514673	-1012						
ANXA10	-1473						
ABCB4	-1516						
MGP	-3524						

Appendix IV Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
AF264621	648.5	TTC39C	17.6	PKD1L2	9.4	DNAJC22	6.6
AF100640	326.4	CGNL1	17.4	DNAJC12	9.4	HIPK2	6.6
TBX15	164.9	SCN7A	16.9	GSTT2	9.4	LRRCC1	6.6
KRT80	150.3	GNG2	16.9	ADAM23	9.3	MIRLET7BHG	6.5
ENOX1	93.5	FAM9C	16.3	GLT1D1	9.2	A_32_P226656	6.5
LOC100132593	89.0	PAPPA	16.2	AKR1C3	9.2	FOXE1	6.4
EPDR1	79.5	LMCD1	16.1	GCLC	9.1	COL16A1	6.3
PERP	76.8	KIAA1377	15.7	ATP1B1	9.0	HSF2	6.3
GALNT14	67.5	RNF128	15.6	CA13	9.0	MMP1	6.3
CNRIP1	61.1	TUBB2B	15.4	MMP3	8.9	AP4E1	6.2
LHX2	57.0	HECA	15.0	EPCAM	8.8	A_23_P91130	6.2
FNDC1	46.2	RNF128	14.8	KIF26B	8.3	FBN1	6.2
PPIC	44.3	AMOTL1	14.7	PLAGL1	8.3	THC2651324	6.2
JAM2	41.7	MYOF	14.5	AUTS2	8.2	FXYD1	6.2
CSGALNACT1	38.8	TGFB2	14.4	ATP1B1	8.2	COL3A1	6.1
LACC1	36.6	KLHL29	14.1	ENST00000537149	8.1	BX094072	6.1
TMEM98	35.4	DLX4	13.9	DENND2C	8.0	ABCA5	6.1
FAM9C	33.7	LCP1	13.8	FEZ1	7.9	PLAT	6.0
TMEM98	29.9	RIPPLY2	13.4	LRRCC1	7.9	MCF2L	5.9
SERPINB1	29.1	OSTF1	13.3	RHOBTB3	7.9	EOMES	5.9
SLC39A8	28.9	C9orf95	13.0	ANG	7.8	LOC728392	5.8
SERPINB9	28.8	HTRA1	12.9	LOC100506059	7.8	BG695979	5.8
PPIC	27.5	L3MBTL3	12.8	HIPK2	7.7	A_32_P181443	5.7
IQGAP2	26.9	A_23_P139166	12.8	ANTXR1	7.7	MYB	5.7
MXRA8	26.1	THC2493376	12.8	SEL1L3	7.7	FAM101A	5.6
DB534761	25.1	DOK6	12.4	A_24_P733345	7.5	RHBDL3	5.6
HOXB13	25.0	GCLC	12.0	PRPH	7.5	C6orf225	5.5
FOXD1	23.5	NAP1L2	12.0	NMU	7.4	SLC7A7	5.5
AKR1C1	23.4	UST	12.0	GSTT2	7.4	TDRD3	5.5
TM4SF4	23.1	LOC389634	11.8	THC2658802	7.2	DSCR6	5.5
EFNA5	22.7	THC2559752	11.0	HIPK2	7.2	OGFRL1	5.4
AKR1C1	22.3	CPE	10.9	TSPAN5	7.1	NRG2	5.4
A_32_P168756	22.3	JUN	10.8	ZNF704	7.1	SMAD9	5.4
RBM24	18.9	TOX2	10.6	HOTAIR	7.1	LOC100499466	5.3
ARNT2	18.8	NR2F2	10.3	STYK1	7.1	MOCOS	5.3
TM4SF1	18.6	PLAU	10.3	TMEM88	7.0	TMEM35	5.2
THC2657737	18.5	PRSS16	10.1	COL3A1	6.9	ZNF184	5.2
F2RL2	18.3	CYP26B1	9.6	ENST00000461931	6.9	DYNLT3	5.2
AK021866	18.2	ZNF704	9.6	TTC39C	6.9	HSF2	5.0
B3GNT5	18.1	PLAC9	9.5	ENST00000551187	6.8	HEBP2	4.9
L3MBTL3	18.1	MBNL2	9.4	FNDC4	6.7	ITM2A	4.9

Appendix IV Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
AL049443	4.8	PRKCA	4.2	NEBL	3.6	CTGF	3.2
TRPM7	4.8	THC2660361	4.1	STON1	3.6	UFM1	3.2
SSH3	4.8	SGK1	4.1	ENST00000323496	3.6	C6orf70	3.2
AMOTL1	4.8	GPRC5C	4.1	SMYD3	3.6	ZFAND4	3.2
PAG1	4.7	FAM184A	4.1	PAPSS2	3.6	CPT1A	3.2
SYCP2	4.7	TGM2	4.1	EYA4	3.6	TCEAL3	3.2
ASPRV1	4.7	CABYR	4.1	TMSB4X	3.6	A_24_P126741	3.2
KIAA1377	4.7	CXorf57	4.0	GLUL	3.5	HEXIM1	3.2
A_32_P145159	4.7	DHDH	4.0	A_24_P530977	3.5	DYNLT1	3.2
TRAF3IP2	4.7	GSTA2	4.0	MMD	3.5	SLC27A2	3.2
FAM43B	4.6	MRAP2	4.0	MAGI2	3.5	CR598370	3.1
PAG1	4.6	GBE1	4.0	SMAD9	3.5	ST7-AS1	3.1
MORC4	4.6	RNF217	4.0	NOS2	3.5	MTMR11	3.1
GABARAPL1	4.6	BQ050540	3.9	NAIP	3.4	ACYP2	3.1
TRPM7	4.5	IFI27L2	3.9	TSPYL4	3.4	TCEAL5	3.1
IFIT2	4.5	AK124841	3.9	C4orf34	3.4	ENST00000423704	3.1
AK094629	4.5	SLC30A3	3.9	COL6A1	3.4	OLFML2A	3.1
DYNLT3	4.5	PCDH10	3.8	MMP10	3.4	LHPP	3.1
COL3A1	4.5	TBXAS1	3.8	NFIB	3.4	TESC	3.1
TMSB15A	4.5	PMP22	3.8	FAM82A1	3.4	SMYD3	3.1
TPBG	4.5	SCHIP1	3.8	BCAS4	3.4	SLC7A11	3.1
PDE9A	4.4	HLA-DMB	3.8	TMSB4X	3.3	S100A4	3.1
CRLF1	4.4	THC2588453	3.8	THC2544198	3.3	A_32_P112546	3.1
SC5DL	4.4	TUBB3	3.8	YPEL5	3.3	TUBB8	3.1
CNTNAP2	4.4	LIPA	3.8	VASH2	3.3	ENST00000424852	3.1
ENST00000411845	4.4	UTRN	3.8	GPRASP2	3.3	AKAP12	3.1
AHNAK	4.4	GABARAPL1	3.8	RAB32	3.3	MXD1	3.1
LTBP1	4.4	NANOS3	3.7	WDFY3-AS2	3.3	F11R	3.0
FBXL7	4.3	NR2F2	3.7	FAM82A1	3.3	SLC7A11	3.0
PTH1R	4.3	SASH1	3.7	IFIT1	3.3	GABARAPL3	3.0
CD9	4.3	PAPSS2	3.7	SOX4	3.3	PSD3	3.0
SC5DL	4.3	MED23	3.7	NKAIN1	3.3	CNKSR3	3.0
DAAM1	4.3	EPAS1	3.7	AK124097	3.3	THC2536014	3.0
RGS20	4.3	RTTN	3.7	F11R	3.3	ENST00000502419	3.0
LOC554207	4.3	HIST1H1A	3.7	NT5DC1	3.3	SGK3	3.0
FKBP1B	4.2	RCAN3	3.7	DKK3	3.3	LOC100288144	3.0
AKAP12	4.2	GLYATL1	3.6	INPP4B	3.2	C1S	3.0
CU679648	4.2	MARK1	3.6	A_32_P96752	3.2	ULK2	3.0
STARD6	4.2	SRCRB4D	3.6	FSTL1	3.2	S100A2	3.0
MYBL1	4.2	GLRX	3.6	PLEKHG5	3.2	HES2	3.0
FERMT1	4.2	CAHM	3.6	DAPK2	3.2	MBOAT1	3.0

Appendix IV Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
C6orf192	3.0	CRYL1	2.8	ENST00000416395	2.6	LMF1	2.5
NEBL	3.0	TMSB4X	2.8	A_24_P187154	2.6	AZI2	2.5
SH3PXD2A	3.0	A_24_P670147	2.8	MORN4	2.6	TIAM2	2.5
TCEAL6	3.0	IL11	2.8	CCNG2	2.6	ENST00000394813	2.5
ADD3	3.0	FYN	2.8	MBL2	2.6	CHMP4C	2.5
LOC554207	3.0	BIRC7	2.8	CBLB	2.6	FUCA1	2.5
AK057652	3.0	CCDC28A	2.8	LOC390705	2.6	CDC40	2.5
TCEA3	2.9	ENST00000449075	2.8	GPR161	2.6	ASAP3	2.5
BC028039	2.9	BC014971	2.8	P4HA2	2.6	LGALSL	2.5
C13orf15	2.9	SNX16	2.8	C9orf125	2.6	ARNTL2	2.5
FKBP7	2.9	EMID1	2.8	ATP8B3	2.6	RECK	2.5
PLOD2	2.9	NAP1L5	2.8	ELOVL3	2.6	ACYP2	2.5
THC2611641	2.9	NDRG4	2.8	ACYP2	2.6	SYTL1	2.5
RAB32	2.9	CTNNBIP1	2.8	TCP1	2.6	SHISA4	2.5
DECR1	2.9	AI669333	2.8	SNX9	2.6	SRSF12	2.5
MICAL1	2.9	C11orf96	2.8	THC2679484	2.6	SLC16A5	2.5
TCP1	2.9	DCBLD1	2.7	LOC730101	2.6	TCP1	2.5
FBXO5	2.9	OSCAR	2.7	AK025975	2.6	PRIM2	2.5
SQRDL	2.9	THC2637707	2.7	SERINC1	2.6	NPNT	2.5
ANKRD58	2.9	PLXDC2	2.7	ICK	2.6	ALS2CR8	2.5
ADD3	2.9	PSMB1	2.7	TIFA	2.6	PELI1	2.5
PARVA	2.9	A_24_P144149	2.7	EYA4	2.6	FAM100B	2.5
ZFHX4	2.9	MEGF6	2.7	TNFRSF25	2.6	FAM195B	2.5
KIRREL2	2.9	DECR1	2.7	FOXA1	2.6	RAB3B	2.5
CDKN1C	2.9	EZR	2.7	OAT	2.6	TMEM237	2.5
PHF10	2.9	BC039411	2.7	FBXO25	2.6	NRG2	2.5
SPARC	2.9	PTRF	2.7	PSD3	2.6	ZNF853	2.5
SPPL2A	2.9	FAM149B1	2.7	SHF	2.6	A_24_P914669	2.4
THC2713545	2.9	LOC100192378	2.7	A_32_P30898	2.6	WTAP	2.4
SSU72	2.8	PROCR	2.7	APOBEC3B	2.6	MEIS1	2.4
GTF2H5	2.8	COLEC12	2.7	CACNA1G	2.6	STXBP5	2.4
KREMEN1	2.8	CEP55	2.7	TSPYL1	2.6	SOX4	2.4
UNC5B	2.8	PRAME	2.7	LRRTM4	2.6	ARHGAP22	2.4
MUC15	2.8	SYTL1	2.7	ABAT	2.6	NUDT7	2.4
PSMB1	2.8	A_24_P229728	2.7	ANXA4	2.5	IGF2R	2.4
TGFBR2	2.8	LOC400099	2.7	EZR	2.5	LOC100287525	2.4
WTAP	2.8	C6orf70	2.7	PTGER2	2.5	BACE1	2.4
MESP1	2.8	PHF14	2.7	PLCD1	2.5	FAS	2.4
PPP1R12B	2.8	CSPG4	2.7	MUM1L1	2.5	RGL3	2.4
LOC389033	2.8	ANK3	2.7	COL6A2	2.5	SERPINB1	2.4
THC2500237	2.8	BMF	2.6	NEURL1B	2.5	THC2642212	2.4

Appendix IV Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
CDC40	2.4	DPYSL2	2.3	AGAP2	2.2	CYTH1	2.1
RGS2	2.4	SLC17A5	2.3	DKK1	2.2	BQ948285	2.1
MRPL18	2.4	IBTK	2.3	MFAP2	2.2	WNT3	2.1
SLC10A4	2.4	FGF21	2.3	KCNIP3	2.2	SLC24A1	2.1
SNX10	2.4	AU147416	2.3	RAB9B	2.2	PLA2G12A	2.1
H6PD	2.4	S73202	2.3	C20orf201	2.2	SH3BP5	2.1
ATP1B2	2.4	ACAT2	2.3	CEP68	2.2	TRIM2	2.1
ARHGEF19	2.4	PPP3CB	2.3	BQ638334	2.2	ASF1A	2.1
THC2559002	2.4	MLH3	2.3	PCYOX1L	2.2	DDAH2	2.1
GNAZ	2.4	OBFC1	2.3	EML4	2.2	OSTM1	2.1
SERPINI1	2.4	KIAA1908	2.3	NBR1	2.2	UBXN2A	2.1
ZDHHC8P1	2.4	BCL6	2.3	FGFR1	2.2	ACSL1	2.1
ACAT2	2.4	SFR1	2.3	HERC4	2.2	UBTD1	2.1
CDC40	2.4	SEPP1	2.3	ASRGL1	2.2	WTAP	2.1
KAZALD1	2.4	RNF157	2.3	C15orf59	2.2	TRAM1L1	2.1
ENST00000458030	2.4	CCDC80	2.3	SFT2D1	2.2	A_24_P178444	2.1
MCF2L	2.4	OSTM1	2.3	PPM1D	2.2	RFTN1	2.1
C6orf72	2.4	COL27A1	2.3	RIMKLB	2.2	KIAA1211	2.1
C1orf170	2.4	MMP11	2.3	ZNF25	2.2	FAM160B1	2.1
TTC7A	2.4	PEX3	2.3	YIPF4	2.2	STXBP5	2.1
HOMER3	2.4	RGN	2.3	A_24_P367100	2.2	THC2638839	2.1
MARVELD1	2.4	WNT5B	2.3	ACOX1	2.2	THC2756581	2.1
SNX16	2.4	TMSB15B	2.3	GPR161	2.2	C11orf70	2.1
AL832534	2.4	WIF1	2.3	LRP12	2.2	NUP43	2.1
IFIT5	2.4	AL833005	2.3	RFFL	2.2	KIAA1107	2.1
COLEC11	2.4	PIGC	2.3	LOC729970	2.2	PINK1	2.1
MORN4	2.4	C9orf125	2.3	A_32_P213389	2.2	LAMC3	2.1
P4HA1	2.3	C9orf93	2.2	LIMS3	2.2	FAM64A	2.1
PCDH15	2.3	MEX3A	2.2	LOC84989	2.2	TMEM181	2.1
GPER	2.3	EML4	2.2	SOD2	2.2	FLJ37453	2.1
CITED1	2.3	SMEK2	2.2	SGCA	2.2	DST	2.1
THC2699069	2.3	PEX7	2.2	FRA10AC1	2.2	A_24_P33055	2.1
MFSD11	2.3	PALM	2.2	DCLK1	2.2	ENST00000513644	2.1
GLCCI1	2.3	THC2667190	2.2	RIPK2	2.2	ATP10A	2.1
FGGY	2.3	ADPRHL1	2.2	LOC100506659	2.2	DUSP26	2.1
ACSF2	2.3	TRIM7	2.2	CCDC104	2.2	MTHFD1L	2.1
METTL7A	2.3	APOBEC3F	2.2	AL833005	2.2	MAPK8	2.1
C6orf211	2.3	PRDM13	2.2	C6orf35	2.1	MEX3A	2.1
TBP	2.3	ARHGEF10L	2.2	COPG2	2.1	C20orf46	2.1
PLCH1	2.3	RPRML	2.2	A_32_P78488	2.1	TULP4	2.1
PDCD2	2.3	SCPEP1	2.2	ARL17A	2.1	SLC16A9	2.1

Appendix IV Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
TUFT1	2.1	GULP1	-2.0	PWWP2B	-2.1	STK25	-2.3
SCN4B	2.1	COQ10A	-2.0	THC2526765	-2.1	A_24_P230288	-2.3
LAPTM4A	2.1	NUDT9	-2.0	TTC13	-2.1	BTN3A2	-2.3
P4HA2	2.1	THC2714184	-2.0	ERO1LB	-2.1	MAPK12	-2.3
ENST00000443631	2.1	DICER1	-2.0	CASP4	-2.1	THC2673265	-2.3
TUBE1	2.1	INSIG2	-2.0	CDK5RAP1	-2.1	PALLD	-2.3
RIPK2	2.1	HELB	-2.0	AA151106	-2.1	ECHS1	-2.3
PIK3R3	2.1	CASP4	-2.0	EFHA2	-2.1	MAPRE1	-2.3
VSIG10L	2.1	ASMTL	-2.0	MACF1	-2.1	PNMAL1	-2.3
SYT6	2.1	THC2496215	-2.0	COG2	-2.1	CKMT1A	-2.3
ARL6IP5	2.1	AK092681	-2.0	DTYMK	-2.1	PPM1F	-2.3
GCHFR	2.1	PLEKHA5	-2.0	ENST00000375673	-2.1	MALT1	-2.3
NOVA1	2.1	A_24_P400702	-2.0	MRPS30	-2.1	IGDCC3	-2.3
RPAIN	2.0	WARS	-2.1	LOC100240735	-2.1	CHML	-2.3
GAS6	2.0	EMP1	-2.1	MYO1E	-2.1	PML	-2.3
ISG20	2.0	MYEF2	-2.1	SNCA	-2.1	OBSCN	-2.3
FAM120B	2.0	TRIM11	-2.1	ENST00000428471	-2.2	PBX3	-2.3
AK098220	2.0	RNF187	-2.1	CAPN10	-2.2	CHODL	-2.3
LOC100287590	2.0	THC2497772	-2.1	MAPRE1	-2.2	FGG	-2.3
GLCE	2.0	DIS3L2	-2.1	SIX4	-2.2	ADAM8	-2.3
PCYOX1	2.0	DGKD	-2.1	ZNF511	-2.2	ASMTL	-2.3
ARHGEF10L	2.0	E2F7	-2.1	CFH	-2.2	THC2682560	-2.3
DEPDC7	2.0	SCO2	-2.1	THAP4	-2.2	DNMT3B	-2.4
USP11	2.0	OSBPL8	-2.1	DGKH	-2.2	ZFHX2	-2.4
ZUFSP	2.0	CISH	-2.1	FRMD6	-2.2	IL1RAPL2	-2.4
B3GNT8	2.0	TRABD	-2.1	KLF6	-2.2	PPP1R7	-2.4
ME1	2.0	KLF6	-2.1	OSR2	-2.2	TRIM11	-2.4
KLF13	2.0	FH	-2.1	DUSP5P	-2.2	ZNF521	-2.4
RPS12	2.0	ZNF398	-2.1	MAPK11	-2.2	DEGS1	-2.4
AKAP7	2.0	CCDC88C	-2.1	MRPS30	-2.2	GPR126	-2.4
AK025716	2.0	DTYMK	-2.1	SLC25A41	-2.2	KIAA1671	-2.4
RWDD1	2.0	FAM155B	-2.1	A_24_P178167	-2.2	ATG4B	-2.4
FCGRT	2.0	ITPRIPL1	-2.1	POSTN	-2.2	CXXC5	-2.4
PCDHB2	2.0	GDNF	-2.1	PSEN2	-2.2	CREB3L2	-2.4
NFE2L1	2.0	CDT1	-2.1	TBC1D4	-2.2	TERT	-2.4
DTNB	2.0	HEATR1	-2.1	GPR89B	-2.2	AA541413	-2.4
CETN3	2.0	RHOU	-2.1	MDFIC	-2.2	SCFD2	-2.4
PEX1	2.0	GMPPB	-2.1	TTLL4	-2.2	SH3BGRL2	-2.4
WDR1	-2.0	PTBP2	-2.1	PPP2R1B	-2.2	LOC151174	-2.4
LOC100240735	-2.0	STK25	-2.1	MIPEP	-2.2	FAIM	-2.4
METTL21A	-2.0	SKIL	-2.1	BC030757	-2.2	LTB	-2.4

Appendix IV Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
RTN4RL1	-2.4	CHD7	-2.8	HLA-G	-3.2	SP140L	-3.8
AF289562	-2.4	AK095300	-2.8	PARP14	-3.2	THC2770932	-3.8
KREMEN2	-2.5	HOXC8	-2.8	FZD5	-3.2	PYGM	-3.8
PLSCR1	-2.5	PUS7L	-2.8	VMO1	-3.3	JAG2	-3.8
A_24_P532730	-2.5	RARRES3	-2.8	UBE2L6	-3.3	CKMT1A	-3.8
AK021614	-2.5	ENST00000485364	-2.8	CNN1	-3.3	HLA-C	-3.9
ENST00000428814	-2.5	SCLY	-2.8	COPS8	-3.3	STX18	-3.9
RUNX2	-2.5	ING5	-2.8	C1orf198	-3.3	HLA-B	-3.9
NDUFA10	-2.5	BHLHE41	-2.8	VPS13A	-3.3	ABCA3	-3.9
CARD17	-2.5	HOXB3	-2.9	LINC00478	-3.3	A_32_P194704	-3.9
ASB1	-2.5	CTSK	-2.9	ENO3	-3.4	HLA-J	-3.9
CHD7	-2.6	CLDN8	-2.9	GSG1	-3.4	BICC1	-4.0
GRB14	-2.6	RANBP17	-2.9	SIPA1	-3.4	HLA-C	-4.0
FRY	-2.6	C10orf125	-2.9	ZNF506	-3.4	HLA-B	-4.1
SDS	-2.6	NGEF	-2.9	SPOCK2	-3.4	RIC3	-4.1
NDUFA10	-2.6	STAU2	-2.9	GPC3	-3.4	NTS	-4.1
CU687617	-2.6	ARMC9	-2.9	GATA5	-3.4	NP111779	-4.1
ING5	-2.6	KLHDC10	-2.9	FW340012	-3.4	FBXL16	-4.1
A_32_P14737	-2.6	IGF1R	-2.9	ARMC9	-3.4	A_32_P1841	-4.1
ANKRD24	-2.6	REC8	-2.9	SOCS3	-3.5	AMIGO2	-4.1
DDX58	-2.6	SLCO4A1	-3.0	THC2700145	-3.5	UGCG	-4.2
CDH9	-2.6	MLF1	-3.0	RIMS2	-3.5	HLA-C	-4.2
PLA2G16	-2.6	ASB1	-3.0	HLA-E	-3.5	UNC13A	-4.2
C10orf125	-2.6	ATP6V0D2	-3.0	BU685399	-3.5	BATF2	-4.2
ZDHHC2	-2.6	UPP1	-3.0	THC2677011	-3.5	RTKN2	-4.2
DPYSL4	-2.6	EPHA3	-3.0	SIK2	-3.5	MET	-4.2
PRKAR1B	-2.7	CARD16	-3.0	FZD5	-3.5	RDH10	-4.3
ENST00000428928	-2.7	ACTG2	-3.0	LPAR3	-3.6	PARP14	-4.3
FBXO16	-2.7	RUNX2	-3.0	HLA-A	-3.6	STX18	-4.4
ISOC1	-2.7	FAM89A	-3.1	ACTN3	-3.6	AA455656	-4.4
STK32C	-2.7	MLF1	-3.1	FBN2	-3.6	A_24_P144134	-4.4
MST4	-2.7	UGCG	-3.1	ADAMTS3	-3.6	HLA-H	-4.4
B2M	-2.7	PML	-3.1	DBNDD2	-3.6	RHOBTB1	-4.4
CHD7	-2.7	THC2675062	-3.1	HLA-A	-3.6	STAT1	-4.4
ZDHHC2	-2.7	DMKN	-3.1	ZFP36L1	-3.7	THC2648509	-4.4
KLHDC10	-2.8	NDUFA10	-3.1	HLA-E	-3.7	RGS16	-4.4
LPAR3	-2.8	MLF1	-3.2	ENST00000519753	-3.7	B3GALT1	-4.4
CXXC5	-2.8	PML	-3.2	SIX1	-3.8	PRKCH	-4.4
WASF3	-2.8	PASK	-3.2	HLA-C	-3.8	SHOX2	-4.4
KLHDC10	-2.8	ANKRD34A	-3.2	RGS16	-3.8	FIBIN	-4.5
HLA-E	-2.8	ZXDA	-3.2	BM928667	-3.8	THC2676635	-4.5

Appendix IV Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
FRMD4A	-4.5	SNCG	-6.9	RNLS	-9.9	BX538139	-15.2
RDH10	-4.6	IGFN1	-6.9	ESRRG	-10.1	AGT	-15.3
C11orf93	-4.6	RASGRP2	-7.1	SLC15A3	-10.2	ADAMTS1	-15.3
SHOX2	-4.6	CLDN17	-7.1	DDX60L	-10.2	CAV1	-15.9
FAM59A	-4.7	TAP1	-7.1	COL6A3	-10.3	FBN2	-16.1
EBI3	-4.8	LMO1	-7.1	GALNT4	-10.4	PDE1A	-16.3
AMOT	-4.8	A_32_P121978	-7.2	IFI27	-10.5	HSPA1A	-16.4
AK094726	-4.8	SEMA6A	-7.2	UPP1	-10.5	THC2628387	-16.5
HLA-F	-4.8	SSFA2	-7.2	GBP3	-10.7	SOX9	-17.2
HLA-B	-4.8	PPP2R2B	-7.2	HES1	-10.8	C7orf58	-17.9
IGFBP2	-4.8	ARID5B	-7.3	SEMA6A	-11.0	HOXB9	-18.0
OCLN	-4.9	AK092921	-7.4	SP100	-11.0	ARHGAP28	-18.2
ENC1	-5.1	CYB5R2	-7.6	HOXD3	-11.2	CBLN2	-18.2
MGST1	-5.1	ZIC1	-7.6	HEY1	-11.3	IRX5	-18.3
POC1B	-5.1	HOXD8	-7.7	ATP2B1	-11.3	BAMBI	-18.5
PLA2G3	-5.2	MAT1A	-7.7	SAA1	-11.4	FAM111B	-18.6
PTH2	-5.3	MSX1	-7.8	XAF1	-11.6	C18orf34	-19.0
A_24_P101771	-5.3	ARMCX2	-7.8	P2RY2	-11.9	NMI	-19.2
RAB3IP	-5.3	DYNC1I1	-7.9	BST2	-11.9	ONECUT1	-19.4
HLA-B	-5.4	DUSP6	-7.9	MT1F	-11.9	HAPLN1	-19.7
STAT1	-5.4	IRF1	-8.0	L3MBTL4	-12.7	HOXD4	-19.9
VPS13A	-5.5	A_23_P314024	-8.1	ALPK2	-12.8	TNMD	-20.0
PARP9	-5.6	GNPDA1	-8.2	ENO2	-12.9	ENST00000507916	-20.4
KANK1	-5.6	THC2704911	-8.2	BEX2	-13.1	A_32_P191141	-20.7
CTSF	-5.6	EPHA7	-8.2	TYRP1	-13.2	TAC1	-20.8
VPS13A	-5.7	ZIC1	-8.3	SEMA3A	-13.2	TES	-20.8
WNT3A	-5.8	HLA-A	-8.4	SEMA6A	-13.3	ELF4	-21.4
ARID5B	-6.0	MSX1	-8.6	SSFA2	-13.3	BM989848	-21.5
A_24_P686243	-6.1	CD40	-8.6	ARPP21	-13.4	A_24_P489649	-21.9
A_32_P100379	-6.1	PSMB9	-8.7	PDGFRA	-13.6	RBPMS	-22.0
THC2520542	-6.1	HLA-H	-8.9	SDC2	-13.7	DCDC5	-22.7
SUSD1	-6.1	SMCR5	-8.9	PPP1R1C	-13.9	HOXB6	-22.8
LAYN	-6.3	SAA2	-9.0	SOX6	-13.9	HES1	-23.6
C5	-6.3	SIX6	-9.3	LAMA1	-13.9	LOC100506674	-23.8
XIRP2	-6.4	DLK1	-9.3	ITGA1	-13.9	ASXL3	-24.1
A_23_P125109	-6.6	BASP1	-9.3	THC2637568	-13.9	IRX5	-26.6
AK022020	-6.6	APOL6	-9.7	TMEM30B	-14.1	CTNNA2	-27.3
MMRN1	-6.6	DGKB	-9.7	TES	-14.1	GBP1	-27.7
DDX60	-6.7	CRB1	-9.7	CASP1	-14.4	LIMCH1	-29.3
GALNT4	-6.8	WNT5A	-9.7	HOXB5	-15.1	IL7	-30.1
AK095791	-6.9	IFI27	-9.8	DIO3	-15.1	POU1F1	-30.4

Appendix IV Gene Expression Changes in $A2780_{CBN\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
GBP1	-30.6	BAALC	-41.1	VAV3	-67.7	FZD8	-94.2
PDE1A	-31.5	ISL1	-41.6	ZFP42	-74.0	CRNDE	-125.4
FBN2	-32.6	HOXB8	-43.0	MEST	-79.1	GPR158	-153.2
L1TD1	-34.8	RSPO2	-48.5	AK129542	-79.1	FLRT3	-214.0
KITLG	-34.9	LAYN	-49.9	SLC27A6	-79.7	PHOX2B	-216.8
NRXN1	-37.8	SLC8A1	-50.5	KANK4	-79.9	PITX2	-237.3
DIRAS3	-38.4	NLGN4X	-50.6	FOXP2	-80.2	PPP1R1C	-317.6
IFNG	-40.0	SEMA3D	-62.7	ENST00000555442	-85.5		
C7orf58	-40.5	IRX3	-66.8	RSPO2	-86.0		

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
GPM6A	1097.1	KANK4	68.2	ENST00000323496	35.0	SOCS3	20.7
DUSP6	949.1	CYP1B1	67.5	SPG20	34.3	ARMC9	20.1
SLC25A24	793.5	CYR61	63.8	DA727827	34.1	ENST00000551107	19.9
RBMS3	530.3	SATB1	62.6	HOXB8	33.7	NEDD4L	19.4
EMP1	506.2	TNFRSF19	59.7	PRKCH	33.2	ARHGAP28	19.2
ANO3	447.2	THC2681889	57.9	IFNG	32.8	FIBIN	18.7
PPP1R1C	383.0	FAM129A	57.6	SDC2	32.0	TAC1	18.7
AK129542	367.4	SEMA3D	57.5	LOXL1	31.4	TNMD	18.6
CCR1	355.7	TMSB4X	56.4	DSEL	31.3	ENST00000555442	18.4
MMP10	262.3	NRIP1	55.9	DIRAS3	30.6	DIO3	18.3
PITX2	220.3	FRY	55.2	CYR61	30.6	ALCAM	18.2
PDGFRA	210.7	MUC15	53.2	ADAMTS1	29.4	NETO1	18.2
ZFP42	179.9	SUN3	51.7	ARHGAP28	28.7	OTOL1	17.8
GPR158	172.1	RNF128	50.0	HSPA1A	28.1	POC1B	17.4
ESRRG	157.1	GSG1	49.4	LOC100505971	27.8	CAV1	17.4
LRRTM4	156.1	AGMO	47.1	NUDT11	27.3	PI15	17.3
A_32_P106615	147.7	TMSB4X	46.1	DPYSL2	26.7	IL21R	17.1
RBMS3	140.4	GRIK1	46.0	IRX5	26.3	GIMAP2	17.1
ZNF521	137.4	FOLH1	45.5	PREX1	26.0	C5	17.1
LRRTM4	127.0	ZNF439	44.5	AGT	26.0	PLXDC2	16.9
LAYN	116.8	GLUL	44.2	SP110	25.8	AK024926	16.6
MDFIC	115.0	RBPMS	43.2	DDAH1	25.2	BCAS4	16.1
HOXB6	113.1	PCDH15	43.0	LIN28A	25.2	POSTN	16.0
TMSB15B	110.2	L1TD1	43.0	SP140	24.9	FLJ35024	16.0
ALPK2	107.4	SH3BP4	42.9	DOCK3	24.6	THC2732175	15.9
GBP1	101.0	COLEC12	42.6	TCEAL6	24.4	SLC16A3	15.7
EYA4	97.4	WNT3A	42.6	GRASP	24.4	TMSB4X	15.7
TMEM30B	96.2	FOXA1	41.6	C11orf75	24.2	BCL6	15.5
CRISPLD1	96.0	LZTS1	41.5	CTNNA2	23.5	FCHO1	15.5
SPG20	94.5	SLIT2	41.2	TLE4	23.5	NEO1	15.3
TMEM47	93.0	NAV3	39.0	PLA2G3	23.5	C4orf32	15.2
NOX4	91.3	TCEAL5	39.0	CLDN17	23.4	CD248	15.1
FOLH1B	89.0	PDGFRB	37.8	ONECUT1	22.9	GLDC	14.9
CXorf57	86.0	NEDD4L	37.6	TLE4	22.4	SLC15A3	14.8
KITLG	85.9	MEOX2	37.5	NTNG1	22.2	CRNDE	14.8
TES	80.6	TCEAL3	37.2	BTNL9	22.2	MBNL3	14.7
MMP3	73.5	FGF20	37.0	SAA1	22.2	FAM171B	14.6
GJA1	72.5	HOXB9	36.3	RBMS3	21.3	PCSK7	14.4
A_24_P530977	69.4	MARCKS	36.1	NFE2	21.2	TRPC4	14.3
MMP1	69.1	TYRP1	35.1	DPYSL2	21.0	NRXN1	14.2
		ARMC9	35.1	TRPS1	20.8		

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
RASIP1	14.0	PDGFA	10.9	A_32_P57717	8.5	LCP1	7.2
INPP4B	14.0	PDE1A	10.8	METRNL	8.5	FAM198A	7.2
GCG	13.7	ADM	10.8	SPARCL1	8.5	THBS1	7.2
SAA2	13.7	ENST00000504916	10.7	BASP1	8.5	AGAP2	7.2
ITGA6	13.4	MID2	10.6	APC2	8.5	PLOD2	7.1
DHRS2	13.4	VMO1	10.6	RGS16	8.4	GATM	7.0
PCDH19	13.0	VLDLR	10.5	FAM89A	8.4	LOC283454	7.0
ZNF585A	13.0	FOXA1	10.5	COL6A3	8.3	SIX4	7.0
ODZ2	13.0	RTKN2	10.4	PNMA2	8.3	FZD5	7.0
PPP1R1C	13.0	RBMS1	10.4	OCLN	8.3	CCR1	7.0
THC2729899	12.9	IFIT3	10.3	LOC100506674	8.2	DDX60L	6.9
TMEM2	12.9	ETV1	10.2	STAT1	8.1	IL17RD	6.9
IFI27	12.7	PTH2	10.2	SCN9A	8.1	PCDHA11	6.9
BATF2	12.7	UBA7	10.1	RCAN1	8.0	CNRIP1	6.9
CYR61	12.7	CD40	10.0	KCNA7	8.0	D4S234E	6.9
MSX1	12.6	ARPP21	10.0	ADRA2C	7.9	FAM155B	6.9
PSMB9	12.5	A_24_P401051	10.0	GAB2	7.9	SCN9A	6.8
PTX3	12.4	FAM102B	9.9	AMOT	7.9	VAMP8	6.8
TNFRSF14	12.3	TCF7L1	9.9	KCNA7	7.9	APC2	6.8
APOL6	12.1	RTN4RL1	9.8	AK092921	7.8	EGR1	6.7
GRB14	12.1	TAGLN	9.8	INA	7.8	ENST00000428928	6.7
WIF1	12.0	AI056399	9.8	A_23_P314024	7.8	TMEM158	6.7
IFI27	12.0	THC2700145	9.8	IFIT1	7.8	TGIF1	6.6
DUSP27	11.6	NRXN1	9.7	CLGN	7.7	ASB2	6.6
HCG23	11.6	TNNC1	9.6	STXBP6	7.7	LMF1	6.6
IRX5	11.4	ETS2	9.6	FAM129A	7.7	ENST00000456585	6.6
FBXO16	11.4	OCLN	9.5	DHRS2	7.6	SCD5	6.5
TLR3	11.4	MET	9.3	ELF3	7.6	ENO3	6.5
MSX1	11.3	EMP1	9.3	SOX9	7.6	CAPS2	6.4
RASGRP2	11.3	HLA-H	9.2	PLAU	7.6	APC2	6.4
L3MBTL4	11.2	LGR4	9.2	RSPO2	7.5	FZD5	6.4
GBP4	11.2	FIGN	9.2	A_32_P106980	7.5	A_32_P207789	6.4
WDR72	11.2	RGS16	9.2	TTC30A	7.5	GDNF	6.4
CRISP1	11.1	FAM171B	9.1	LRFN5	7.5	TRIML2	6.4
GRRP1	11.1	RSPO2	9.1	FJX1	7.4	HSD17B11	6.4
SOX6	11.1	EPHA10	9.1	NES	7.4	PAG1	6.4
CASP1	11.0	TAP1	9.0	SYTL4	7.4	TMEM150C	6.4
PLCL2	11.0	SNCG	8.8	IL1RAPL2	7.4	MALT1	6.4
HEY1	10.9	RBMS1	8.7	C8orf51	7.3	PNOC	6.3
CNDP1	10.9	MDFIC	8.6	PDGFC	7.3	PDE1A	6.3
KIF1A	10.9	HLA-A	8.5	MAT1A	7.3		

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
TCF15	6.2	THC2675062	5.4	HMMR	4.7	ERV9-1	4.2
HSD17B11	6.2	ZFP36L1	5.3	ISG15	4.7	C11orf88	4.2
HIF3A	6.2	SWAP70	5.3	ITGAV	4.6	MEF2C	4.1
LRRFIP1	6.2	SH3D21	5.3	DBNDD2	4.6	DTX3L	4.1
TRIM53P	6.2	TTC30A	5.3	FIGN	4.6	THC2672257	4.1
COTL1	6.2	CD47	5.3	RDH10	4.6	LOC728875	4.1
IRF9	6.2	CARD10	5.3	THC2651023	4.6	PLK5	4.1
EFNA5	6.1	RIPK2	5.3	SGOL1	4.6	BC028022	4.1
CAV1	6.1	IGFN1	5.3	SIPA1	4.6	RTN4R	4.1
PTRF	6.1	CLEC11A	5.2	RAPH1	4.6	ETV4	4.1
STAT1	5.9	SWAP70	5.2	UCP2	4.5	ACPL2	4.1
MYEF2	5.9	EGFR	5.2	PYGM	4.5	KIF16B	4.1
PHC1	5.9	PRPH2	5.2	HLA-C	4.5	ZNF506	4.1
CACNG7	5.9	KREMEN2	5.2	BUB1	4.4	SORT1	4.1
BOD1L	5.9	SLC2A14	5.2	CORO1A	4.4	DEPDC4	4.1
OSGIN2	5.8	TRIM64	5.1	MME	4.4	BQ933774	4.1
RDH10	5.8	ARHGEF16	5.1	AK055647	4.4	KIAA1274	4.0
SPOCK2	5.8	ENST00000538264	5.1	ETV4	4.4	TEX19	4.0
ANGPTL2	5.7	CRABP2	5.0	CCRL2	4.4	IL20RB	4.0
THC2755690	5.7	DACT3	5.0	KLHDC9	4.4	TAGLN	4.0
A_23_P125109	5.7	JPH3	5.0	HLA-B	4.4	ENST00000539135	4.0
FHL2	5.7	COL17A1	5.0	ITGAV	4.3	OTX1	4.0
C1QTNF6	5.7	IGSF9	4.9	PKP3	4.3	ANXA2	4.0
IGFLR1	5.7	ST8SIA1	4.9	HIST1H4L	4.3	SPC25	4.0
SLC6A6	5.6	HEYL	4.9	HIST1H4C	4.3	RPH3AL	4.0
DNMT3B	5.6	UNC13A	4.9	DIAPH3	4.3	PARP14	4.0
ENST00000485364	5.6	GAS2L3	4.9	LOC728855	4.3	FUT1	4.0
AMOTL2	5.5	PARP9	4.9	CSPG4	4.3	MME	4.0
A_32_P100379	5.5	C1orf198	4.9	EFR3B	4.3	HIST1H2AB	4.0
TMCC3	5.5	C2CD4C	4.9	HIST1H4B	4.3	RCOR3	4.0
HTR7	5.5	EPS8L1	4.9	HLA-J	4.3	HIST1H4D	4.0
LOX	5.5	MAGI3	4.8	SNX16	4.2	ANXA2P3	3.9
COTL1	5.5	BC038432	4.8	CXXC5	4.2	CBX5	3.9
ERC2	5.5	IRF1	4.8	CORO2A	4.2	SLC48A1	3.9
STAU2	5.5	ZNF507	4.8	PRR11	4.2	ATP2B1	3.9
H19	5.5	E01979	4.8	HEBP1	4.2	FXYD5	3.9
GNB5	5.4	HLA-C	4.8	ZNF704	4.2	GPC6	3.9
SNX16	5.4	FXYD5	4.7	PLAUR	4.2	THC2756939	3.9
EPHA7	5.4	C11orf96	4.7	MST4	4.2	RAB3IP	3.9
GALNTL1	5.4	MYLK	4.7	TCF4	4.2	C7orf74	3.9
TSPAN5	5.4	TBC1D12	4.7	GPR162	4.2	A_32_P21742	3.9

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
HLA-B	3.9	CPNE8	3.6	FAM176B	3.4	PIK3CA	3.2
EHBP1L1	3.9	LOC400043	3.5	MT2A	3.4	CCR10	3.2
LOC100131733	3.9	HGF	3.5	NUDT14	3.3	FAM57B	3.2
CENPI	3.8	MEIS3	3.5	RTN4RL2	3.3	THC2707492	3.2
A_24_P101771	3.8	RNFT2	3.5	C19orf66	3.3	RAPH1	3.2
THC2637858	3.8	TLN2	3.5	STAU2	3.3	FRMD6	3.2
FW340012	3.8	ANXA2	3.5	LOC100289361	3.3	FZD2	3.2
KCNG1	3.8	H1F0	3.5	CBX5	3.3	SEC61A2	3.2
ENST00000415104	3.8	EIF5A2	3.5	CFD	3.3	SIX1	3.2
C14orf167	3.8	RNFT2	3.5	MT2A	3.3	HLA-B	3.2
CDC42EP3	3.8	NUDT10	3.5	SRCIN1	3.3	LOC84989	3.2
CGN	3.8	MYL12B	3.5	TBXA2R	3.3	RMI2	3.2
SLC2A3	3.8	ANXA2	3.5	RASL11B	3.3	NP111779	3.2
TMC6	3.8	SAMD13	3.5	MT2A	3.3	NEURL1B	3.2
SLC39A4	3.7	THC2616195	3.5	RAB27A	3.3	ENST00000507916	3.2
MALT1	3.7	ARG2	3.5	ADNP2	3.3	LOC100288675	3.2
THC2603239	3.7	IQCD	3.5	ANXA2P1	3.3	PPP6C	3.2
A_32_P19797	3.7	ERAP2	3.5	HLA-B	3.3	A_32_P161140	3.1
C1orf187	3.7	ERBB2	3.5	BRF1	3.3	FSD1	3.1
BC034319	3.7	PLSCR1	3.5	IVNS1ABP	3.3	ENST00000432751	3.1
FAM122C	3.7	MCAM	3.4	TRIB3	3.3	B3GNT2	3.1
C14orf109	3.7	KLHL5	3.4	NR4A1	3.3	RADIL	3.1
AK054718	3.7	GADD45B	3.4	EPB41L5	3.3	MT1L	3.1
A_32_P60687	3.7	HDX	3.4	A_32_P42895	3.3	A_24_P255123	3.1
CPEB1	3.7	ABCC6	3.4	AK026418	3.3	METTL21A	3.1
PTBP3	3.7	TUBB3	3.4	CENPA	3.3	KIF1B	3.1
RAB3D	3.7	SYNGR3	3.4	C18orf56	3.3	SAMD14	3.1
HLA-G	3.6	TRIB1	3.4	USP18	3.3	PSME2	3.1
PPP2R1B	3.6	IFT81	3.4	HLA-A	3.3	MYADM	3.1
DLGAP5	3.6	EPN3	3.4	GPR107	3.3	WFIKKN1	3.1
BOLA1	3.6	EXTL2	3.4	NUPR1	3.2	KHDC1	3.1
C16orf55	3.6	THC2596442	3.4	BICD1	3.2	RARRES3	3.1
VSIG10	3.6	PML	3.4	OGG1	3.2	ZSCAN2	3.1
A_32_P65157	3.6	CRADD	3.4	THC2638839	3.2	LOC344967	3.1
PHF21B	3.6	PVRL2	3.4	IL4R	3.2	SPRED1	3.1
C18orf54	3.6	HLA-H	3.4	C12orf53	3.2	BRIP1	3.1
PPM1F	3.6	ARVCF	3.4	LOC100505894	3.2	TBC1D1	3.1
BAI1	3.6	VASN	3.4	ACOT7	3.2	S73202	3.1
MAP7D2	3.6	LRRN3	3.4	ASPM	3.2	HLA-C	3.1
LRRC8C	3.6	KRTAP7-1	3.4	MAPK11	3.2	PML	3.1
COTL1	3.6	RIPK2	3.4	IRX3	3.2		

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
EMP2	3.1	MIR17HG	2.9	H2AFJ	2.8	KIF20A	2.7
RAB3D	3.1	LRRC20	2.9	ENST00000535363	2.8	SNX5	2.7
CENPK	3.1	BCL2L12	2.9	SPATA6	2.8	ASPM	2.7
ZNF618	3.1	SLC35G1	2.9	DTX3L	2.8	ELL3	2.7
BC018626	3.1	SOX2	2.9	VSIG10L	2.8	A_24_P418744	2.7
LOC729887	3.1	COL1A1	2.9	DIAPH3	2.8	A_32_P57002	2.7
AK128413	3.1	SREBF1	2.9	CKM	2.8	BU602485	2.7
RANBP17	3.1	PALM3	2.9	HLA-E	2.8	BM928667	2.7
UBE2L6	3.1	SNHG10	2.9	DIAPH3	2.8	TMEM123	2.7
KLHL5	3.1	NPHP1	2.9	MDM1	2.8	CBX7	2.7
GYG2	3.0	PTBP3	2.9	ABCA3	2.8	SH3PXD2B	2.7
GPR20	3.0	MCM3AP-AS1	2.9	SNHG13	2.8	C19orf28	2.7
BC010544	3.0	MNAT1	2.9	EPDR1	2.8	IMPA1	2.7
MT1G	3.0	AF086154	2.9	ENST00000442130	2.8	CDC45	2.7
AB593167	3.0	HOXC8	2.9	MAPKAPK3	2.8	ELK3	2.7
C12orf48	3.0	TNFRSF12A	2.9	ANGPTL4	2.8	MPST	2.7
HLA-F	3.0	ZC4H2	2.9	IGDCC3	2.8	KLRG2	2.7
SOCS2	3.0	INSIG2	2.9	SGCA	2.8	SLC25A21	2.7
METTL21A	3.0	ZC3H15	2.9	KCNH2	2.8	ESCO2	2.7
NOS2	3.0	C14orf142	2.9	BI832578	2.8	CXorf61	2.7
C21orf30	3.0	UGCG	2.9	NT5C2	2.8	KDSR	2.7
A_32_P15169	3.0	FADS2	2.9	FZD3	2.8	OBSCN	2.7
DIAPH3	3.0	MAPK12	2.9	GSTT2	2.8	SCAMP5	2.7
MT1H	3.0	TRIM49	2.9	PAWR	2.8	CXXC5	2.7
CU687617	3.0	BEND4	2.9	PPP6C	2.8	CRIP2	2.7
OSR2	3.0	CKB	2.9	COLEC11	2.8	C12orf62	2.7
IER5L	3.0	C10orf76	2.9	AL832534	2.8	GFPT2	2.7
KCNJ4	3.0	PNPLA6	2.9	VEGFB	2.8	MIS18BP1	2.7
CBX7	3.0	ZFP36	2.9	DDX46	2.8	NCS1	2.7
MT1X	3.0	SIGIRR	2.9	B2M	2.8	RELL2	2.7
HLA-E	3.0	KIF11	2.9	FERMT2	2.7	CRYZ	2.7
NGEF	3.0	EMP2	2.8	KDSR	2.7	NANOS1	2.7
BC010544	3.0	KIRREL	2.8	CREB3L2	2.7	PLEKHG2	2.7
CDC25C	2.9	LOC344967	2.8	U88048	2.7	KAZN	2.7
HLA-C	2.9	MPDZ	2.8	DYNC2H1	2.7	KLF6	2.7
HLA-DPA1	2.9	C5orf4	2.8	ROM1	2.7	CENPF	2.6
POLA1	2.9	ITSN1	2.8	LOC100507507	2.7	KIF18A	2.6
THC2638025	2.9	EFNA4	2.8	SS18L2	2.7	PAIP2	2.6
ID4	2.9	PML	2.8	DDT	2.7	SRGAP2	2.6
RB1	2.9	BST2	2.8	REC8	2.7	MYLPF	2.6
PARD3	2.9	C5orf13	2.8			MORC4	2.6

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
RIN1	2.6	DHFR	2.5	A_32_P205350	2.5	FANCL	2.4
TRIM37	2.6	SLC45A3	2.5	AGGF1	2.5	CCDC88C	2.4
THC2689241	2.6	PBX3	2.5	MYOF	2.5	BRCA1	2.4
LOC344595	2.6	GPRIN1	2.5	GRTP1	2.5	KDM3A	2.4
AA812298	2.6	TIGD2	2.5	RSU1	2.5	LGALSL	2.4
IFT57	2.6	DARS2	2.5	WWC2	2.5	POLD3	2.4
ZFP106	2.6	CUL5	2.5	ACYP2	2.5	DEPDC1B	2.4
COMTD1	2.6	A_24_P230288	2.5	BMI1	2.5	A_32_P167592	2.4
CUBN	2.6	STK39	2.5	MBOAT2	2.5	SLC44A1	2.4
MT1B	2.6	PIF1	2.5	PDE4D	2.5	BTN3A2	2.4
MYO19	2.6	CFH	2.5	ARHGAP44	2.5	TBC1D9	2.4
KLHL5	2.6	PRKD2	2.5	DOCK1	2.5	LIX1L	2.4
ATXN3	2.6	CTDSPL	2.5	RASGEF1A	2.4	A_24_P383934	2.4
CARHSP1	2.6	RASSF4	2.5	NOC3L	2.4	HS1BP3	2.4
KIF26A	2.6	WDR62	2.5	STK39	2.4	ZFAND6	2.4
RELL1	2.6	VCX	2.5	A_24_P84711	2.4	CENPE	2.4
HIP1	2.6	KIAA0586	2.5	RASL10A	2.4	ALMS1	2.4
RPGR	2.6	TCF4	2.5	A_24_P178444	2.4	BC141946	2.4
LXN	2.6	HIST1H2BD	2.5	PAOX	2.4	HSPB11	2.4
CITED4	2.6	FAM46B	2.5	IFITM3	2.4	PEAK1	2.4
KHK	2.6	ISYNA1	2.5	CASP7	2.4	ST6GAL1	2.4
MTBP	2.6	HLA-A	2.5	NAT6	2.4	CHD6	2.4
FHOD1	2.6	CASK	2.5	CTNND1	2.4	TPM1	2.4
UHRF1	2.6	ZDHHC2	2.5	TSPAN6	2.4	C19orf66	2.4
NUDT8	2.6	ZNF33A	2.5	HIST1H2AE	2.4	HIST2H2AC	2.4
USP12	2.6	ABR	2.5	PJA1	2.4	ELMO2	2.4
PLEKHO1	2.6	A_23_P170719	2.5	SMA5	2.4	STAT6	2.4
SPICE1	2.6	PSMB10	2.5	C2orf68	2.4	NRTN	2.4
SLC2A6	2.6	MITD1	2.5	WWTR1	2.4	ANK3	2.4
CASK	2.6	LOC100287177	2.5	DEPDC1	2.4	HIST1H1D	2.4
VCX2	2.6	RGPD2	2.5	WDR41	2.4	XPNPEP3	2.4
C16orf48	2.6	HLA-E	2.5	ENST00000375678	2.4	WDHD1	2.4
AA158952	2.6	KIF14	2.5	UGCG	2.4	THC2526765	2.4
FAM123B	2.6	KIF1A	2.5	PDLIM2	2.4	S1PR2	2.4
FLJ36000	2.6	A_32_P156746	2.5	GADD45B	2.4	SGTB	2.4
LRRC32	2.6	A_24_P306814	2.5	TSPAN14	2.4	CEP55	2.4
RBBP9	2.5	LINC00339	2.5	KDM3A	2.4	C10orf140	2.4
PLEKHF1	2.5	RPL22L1	2.5	CU686711	2.4	C1orf96	2.4
ARID3A	2.5	SH2D4A	2.5	SNX10	2.4	ACOT9	2.4
SOCS2	2.5	TSPAN6	2.5	GMFG	2.4	TSPAN4	2.4
HDAC7	2.5	JUP	2.5	NUCKS1	2.4	A_32_P14737	2.4

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
FAM114A1	2.4	ZNF780B	2.3	BMI1	2.2	PSRC1	2.2
PEX2	2.3	MBTD1	2.3	NSMCE4A	2.2	CDK1	2.2
CNN1	2.3	C12orf47	2.3	NUF2	2.2	GNPNAT1	2.2
FZR1	2.3	BCL3	2.3	STMN1	2.2	A_24_P332953	2.2
RBM4	2.3	MEF2BNB	2.3	THC2645562	2.2	PELI3	2.2
NLGN1	2.3	POLE4	2.3	S100A4	2.2	GBE1	2.2
ENST00000451939	2.3	PPP1R13L	2.3	C1S	2.2	FANCG	2.2
STMN3	2.3	BAD	2.3	FLJ37453	2.2	A_23_P14432	2.2
ITGB3BP	2.3	C18orf34	2.3	TMEM69	2.2	A_32_P52144	2.2
HHEX	2.3	SSSCA1	2.3	PLA2G16	2.2	RASSF2	2.2
FUT8	2.3	SDC4	2.3	EFHA2	2.2	UGP2	2.2
MBOAT2	2.3	CHMP3	2.3	LRR1	2.2	LOC389634	2.2
ACYP1	2.3	PPP2R1B	2.3	XRCC1	2.2	TTC25	2.2
WBP5	2.3	THC2689749	2.3	TESC	2.2	FGFR1	2.2
ZRANB3	2.3	A_32_P16625	2.3	RBFA	2.2	ZNF395	2.2
CCDC40	2.3	RALGAPA2	2.3	BRIP1	2.2	DSCC1	2.2
TIPARP	2.3	A_32_P152696	2.3	LOC440292	2.2	ZNF385A	2.2
A_24_P7040	2.3	VPS29	2.3	SLC38A9	2.2	MCEE	2.2
MITF	2.3	KLF2	2.3	MESDC1	2.2	TK1	2.2
IFITM1	2.3	FANCI	2.2	PI4K2B	2.2	PARD6G	2.2
IFITM2	2.3	A_32_P30320	2.2	H2AFJ	2.2	HPS3	2.2
KIAA0101	2.3	ACOT9	2.2	PML	2.2	STX10	2.2
AARSD1	2.3	CORT	2.2	SDF2L1	2.2	CEP128	2.2
IMPA1	2.3	RP2	2.2	NUDT14	2.2	ITPR1	2.2
WHSC1	2.3	PFKFB4	2.2	KATNAL1	2.2	COMMD4	2.2
LOC400027	2.3	LNPEP	2.2	C14orf119	2.2	MYC	2.2
THC2657931	2.3	LRRC42	2.2	PIGC	2.2	HDAC7	2.2
SEMA6D	2.3	RCBTB1	2.2	BG327427	2.2	TCF7	2.1
RAP2C	2.3	C21orf90	2.2	SHISA5	2.2	HIST2H2AC	2.1
CCNB1	2.3	HAS3	2.2	C21orf58	2.2	VPS13A	2.1
CU690915	2.3	SPATA6	2.2	SAP130	2.2	CCNE1	2.1
C16orf93	2.3	USP6NL	2.2	IVNS1ABP	2.2	B3GALTL	2.1
IKZF4	2.3	SIPA1L3	2.2	CTDSPL2	2.2	ECT2	2.1
KLF11	2.3	IER3	2.2	LIMD2	2.2	PNKD	2.1
CCR5	2.3	FAM107B	2.2	MBOAT2	2.2	COMMD3	2.1
A_23_P216071	2.3	ENST00000430664	2.2	CACYBP	2.2	RASSF3	2.1
SOAT1	2.3	BC013798	2.2	PLCB3	2.2	CDS2	2.1
KIAA1671	2.3	HIST1H4E	2.2	BX107836	2.2	KIAA1704	2.1
HPS1	2.3	TDP1	2.2	APOL2	2.2	RRP1B	2.1
FAM100A	2.3	SMC2	2.2	POLD3	2.2	ZNF695	2.1
GCC2	2.3	PDCL	2.2	CXXC4	2.2	BG612665	2.1

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
GPC1	2.1	ZBTB44	2.1	ZMYM6NB	2.1	OIP5	2.0
TIA1	2.1	IER2	2.1	TYRO3	2.1	SAC3D1	2.0
A_32_P159289	2.1	SREBF1	2.1	RAI14	2.1	SORD	2.0
THC2505678	2.1	AP3B1	2.1	JDP2	2.1	ARHGAP11A	2.0
PLEKHJ1	2.1	SEC61A2	2.1	COMMD4	2.1	FOXE1	2.0
TUBB6	2.1	SPSB3	2.1	FABP5	2.1	SPAG5	2.0
PHTF1	2.1	ZXDA	2.1	NEK2	2.1	VPS29	2.0
KDM3A	2.1	DEPDC1	2.1	HRSP12	2.1	LOC100287628	2.0
ARL5B	2.1	THC2648759	2.1	CABLES1	2.1	SRBD1	2.0
KCTD17	2.1	THC2505678	2.1	B3GNT1	2.1	UBTD1	2.0
DICER1-AS	2.1	CDCA2	2.1	CKS2	2.1	LATS2	2.0
ICAM3	2.1	HOXC8	2.1	FABP5	2.1	MYO5A	2.0
CA14	2.1	C21orf91	2.1	C21orf91	2.1	ILK	2.0
ACVR1	2.1	MMP15	2.1	C8orf58	2.1	WDR34	2.0
ATXN3	2.1	WBP4	2.1	MYO5A	2.1	GRAMD1A	2.0
CERK	2.1	AS3MT	2.1	INF2	2.1	BDP1	2.0
A_32_P44139	2.1	DOK4	2.1	DIEXF	2.1	YAF2	2.0
CBX5	2.1	APOOL	2.1	C12orf76	2.1	CREB3L4	2.0
DZIP1L	2.1	LMNB1	2.1	DOCK7	2.1	NPL	2.0
RTEL1	2.1	HOXB3	2.1	DHRS11	2.1	ENSA	2.0
ECT2	2.1	ADAM19	2.1	GALE	2.0	APEH	2.0
RPL39L	2.1	FANCI	2.1	TMOD3	2.0	ZNF217	2.0
XRCC4	2.1	OBSCN	2.1	THC2619545	2.0	ALAD	2.0
HIST1H2AM	2.1	BCL2A1	2.1	HSD17B1	2.0	MSL3P1	2.0
ARID3B	2.1	CYBRD1	2.1	PLK1	2.0	TMEM102	2.0
POLD1	2.1	ZNF33A	2.1	HPS3	2.0	C4orf3	2.0
OXCT1	2.1	KNTC1	2.1	NCAPD2	2.0	C11orf82	2.0
TPM3	2.1	C14orf28	2.1	H2AFZ	2.0	C10orf47	2.0
FAM20C	2.1	UBE2C	2.1	C16orf57	2.0	LOC442421	2.0
FABP5	2.1	GINS1	2.1	CPSF3	2.0	RIMKLB	2.0
DHFR	2.1	C10orf57	2.1	RNF26	2.0	ING1	2.0
TRIB3	2.1	ABI2	2.1	CYBRD1	2.0	MRPL52	2.0
DHFRL1	2.1	KRAS	2.1	G2E3	2.0	IFITM3	2.0
IFITM4P	2.1	SHC1	2.1	TMSB15A	2.0	CDH18	2.0
ARL5B	2.1	HES4	2.1	DDX52	2.0	P2RY2	2.0
B9D1	2.1	ASCC1	2.1	CDK2AP2	2.0	ACVR2B	2.0
FANCI	2.1	MED11	2.1	PBK	2.0	XM_002343200	2.0
TSPAN4	2.1	FABP5	2.1	CHST7	2.0	ASRGL1	2.0
BRCA2	2.1	KIAA1958	2.1	AK054902	2.0	A_32_P182135	2.0
TBCD	2.1	NEK2	2.1	TMEM126B	2.0	C7orf26	-2.0
SLC9A6	2.1	GPR162	2.1	PROCA1	2.0	ENST00000491977	-2.0

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SNHG8	-2.0	PVR	-2.0	A_24_P152793	-2.1	C10orf118	-2.1
MUL1	-2.0	CUL1	-2.0	PHF2	-2.1	DOLPP1	-2.1
AF354444	-2.0	RNPEP	-2.0	AK026168	-2.1	RBM38	-2.1
A_24_P161655	-2.0	CLK1	-2.1	C1orf162	-2.1	C6orf203	-2.1
RBAK	-2.0	CYTH2	-2.1	ZNF282	-2.1	SLC35E1	-2.1
GANAB	-2.0	SURF6	-2.1	LOC400099	-2.1	PMS2	-2.1
USP22	-2.0	A_24_P332780	-2.1	GOLGA3	-2.1	ZNF721	-2.1
EEF1A1	-2.0	QRSL1	-2.1	CD63	-2.1	FEZ1	-2.1
GATC	-2.0	CCNL2	-2.1	A_32_P106246	-2.1	C7orf49	-2.1
BTN2A1	-2.0	ACAP1	-2.1	PRPF39	-2.1	ZNF174	-2.1
PURB	-2.0	KIAA0090	-2.1	KIAA0889	-2.1	BAG1	-2.1
SNCA	-2.0	KLF9	-2.1	MKRN1	-2.1	SETD1B	-2.1
GSTM4	-2.0	EIF3F	-2.1	NOP56	-2.1	USP7	-2.1
PRMT5	-2.0	GPAM	-2.1	METTL9	-2.1	C2orf28	-2.1
ENST00000378337	-2.0	MAGED1	-2.1	ARF5	-2.1	COX1	-2.1
IST1	-2.0	SRP19	-2.1	CDC42BPG	-2.1	GPC2	-2.1
POMZP3	-2.0	STK19	-2.1	WRNIP1	-2.1	RBM5	-2.1
A_24_P41890	-2.0	MAP3K4	-2.1	HDAC9	-2.1	HPX-2	-2.1
N4BP2L2	-2.0	PPIA	-2.1	EIF5	-2.1	TMSB10	-2.1
PDCD2	-2.0	CBWD5	-2.1	A_32_P173122	-2.1	ASF1A	-2.1
PHF23	-2.0	SLC39A7	-2.1	LINC00174	-2.1	CCDC132	-2.1
BC011779	-2.0	TBCC	-2.1	NUS1	-2.1	C10orf2	-2.1
AK097166	-2.0	UNKL	-2.1	KCTD15	-2.1	MTHFD1L	-2.1
NOMO1	-2.0	AK021777	-2.1	ANKRD18A	-2.1	ODC1	-2.1
THC2526647	-2.0	LOC100510011	-2.1	SYTL1	-2.1	CD9	-2.1
TMX4	-2.0	ZNF434	-2.1	ENST00000439904	-2.1	SLC35F2	-2.1
GOLGA1	-2.0	C3orf51	-2.1	MSX2P1	-2.1	THC2693923	-2.1
VCP	-2.0	MTUS1	-2.1	TCP1	-2.1	KEAP1	-2.1
OSTM1	-2.0	WIPF3	-2.1	EP300	-2.1	SLC4A3	-2.1
LOC100499177	-2.0	PEX12	-2.1	MAN2C1	-2.1	ZNF519	-2.1
FASTK	-2.0	RIMS2	-2.1	PRKY	-2.1	THEG	-2.1
SCN4B	-2.0	ACADVL	-2.1	ASPH	-2.1	ZNF140	-2.1
PURA	-2.0	A_24_P565503	-2.1	TTLL11	-2.1	MRPL32	-2.1
SNORA70	-2.0	GOLM1	-2.1	FV159898	-2.1	PABPC4	-2.1
THC2570021	-2.0	A_24_P852099	-2.1	RBM8A	-2.1	TMEM38B	-2.1
C7orf50	-2.0	A_32_P17615	-2.1	NUDCD3	-2.1	PMS2	-2.1
AK057088	-2.0	RASSF1	-2.1	MOSPD1	-2.1	A_24_P370484	-2.1
TXNIP	-2.0	E2F4	-2.1	MIAT	-2.1	A_32_P85230	-2.1
MDM2	-2.0	RBM25	-2.1	INSIG1	-2.1	ENST00000424133	-2.2
RALGDS	-2.0	ARHGAP17	-2.1	TYW1	-2.1	AK056630	-2.2
HIST1H2BB	-2.0	DNAJC11	-2.1	ZBED1	-2.1	TSHZ1	-2.2

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
HSPB1	-2.2	RBM4	-2.2	GTPBP5	-2.2	CLK1	-2.3
ASB13	-2.2	ZNF498	-2.2	MGC23284	-2.2	CCDC78	-2.3
CCDC153	-2.2	RASA4	-2.2	PSPH	-2.2	BRP44L	-2.3
A_24_P549518	-2.2	FASTK	-2.2	ZNF764	-2.2	LOC100505794	-2.3
MEPCE	-2.2	QPRT	-2.2	DTNBP1	-2.2	THC2701422	-2.3
AFG3L2	-2.2	AF187554	-2.2	ILF3	-2.2	BCL7B	-2.3
ACBD7	-2.2	ENST00000486256	-2.2	RABGEF1	-2.2	SLC35B2	-2.3
ETNK2	-2.2	PPP1R12A	-2.2	NCDN	-2.2	POM121	-2.3
UHMK1	-2.2	BC031320	-2.2	HSPB1	-2.2	NOB1	-2.3
AI198876	-2.2	PSAP	-2.2	PURB	-2.2	FKBP7	-2.3
AF126109	-2.2	SRRT	-2.2	A_24_P814246	-2.2	SHPRH	-2.3
A_24_P110601	-2.2	ARHGAP17	-2.2	XIST	-2.2	LOC440356	-2.3
HSPB1	-2.2	SAP30	-2.2	ZMAT3	-2.2	AKIRIN2	-2.3
AFG3L1P	-2.2	POMZP3	-2.2	AK127081	-2.2	VTA1	-2.3
AY033611	-2.2	SULT4A1	-2.2	RBM8A	-2.3	RALGDS	-2.3
PILRB	-2.2	BANP	-2.2	CLK2	-2.3	THC2660977	-2.3
ARMC5	-2.2	UHMK1	-2.2	AK127572	-2.3	ENST00000532936	-2.3
ZNF322	-2.2	ZSCAN18	-2.2	A_32_P212654	-2.3	DLST	-2.3
RPF2	-2.2	ZNF184	-2.2	RIC3	-2.3	PDPK1	-2.3
CTSB	-2.2	RAB36	-2.2	PHF10	-2.3	FEM1A	-2.3
HNRNPAB	-2.2	PDIA2	-2.2	BANP	-2.3	CRTC3	-2.3
TNPO3	-2.2	SNX13	-2.2	FAM3C	-2.3	LTV1	-2.3
SLC46A1	-2.2	C14orf79	-2.2	AW964144	-2.3	MRS2	-2.3
SLC39A10	-2.2	TP73-AS1	-2.2	METTL21A	-2.3	PILRA	-2.3
POPDC3	-2.2	MAN2B2	-2.2	C7orf31	-2.3	CCDC80	-2.3
PGAP3	-2.2	AM181370	-2.2	GTF2I	-2.3	CYCS	-2.3
LRPAP1	-2.2	EPC1	-2.2	RING1	-2.3	VCP	-2.3
GBA2	-2.2	SEC63	-2.2	PIGS	-2.3	CHN1	-2.3
ND6	-2.2	GOLGA1	-2.2	UBQLN4	-2.3	PTP4A1	-2.3
C14orf149	-2.2	SRI	-2.2	BAX	-2.3	WBP1	-2.3
A_32_P12282	-2.2	ACAP3	-2.2	METTL21A	-2.3	THC2554861	-2.3
OXR1	-2.2	POLR1C	-2.2	A_24_P288993	-2.3	PAQR6	-2.3
A_24_P272073	-2.2	KIF7	-2.2	A_24_P75840	-2.3	C9orf9	-2.3
PNMAL1	-2.2	WDR82	-2.2	ASCC3	-2.3	CYCS	-2.3
ACTR3B	-2.2	DHRS7	-2.2	NOC2L	-2.3	CLDN15	-2.3
RPS2	-2.2	CBX6	-2.2	BCL2L11	-2.3	LOC730102	-2.3
LOC338620	-2.2	ZNF689	-2.2	GPR135	-2.3	C8orf33	-2.3
HIST1H2BO	-2.2	BAZ1B	-2.2	C14orf102	-2.3	THC2554943	-2.3
TCF7L2	-2.2	HBP1	-2.2	A_23_P124177	-2.3	ND1	-2.3
FUCA2	-2.2	ADAMTS13	-2.2	PGAP1	-2.3	RBBP6	-2.3
FAM200A	-2.2	NGRN	-2.2	EPB41L2	-2.3	CD164	-2.3

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
AGAP3	-2.3	LARP1	-2.4	GPCPD1	-2.4	METTL9	-2.5
FAM3C	-2.3	RNF34	-2.4	FAM3C	-2.4	ING3	-2.5
EEF2	-2.3	AL833005	-2.4	SERPINB6	-2.4	PMS2	-2.5
C9orf125	-2.3	GARS	-2.4	BAIAP2L1	-2.5	NQO1	-2.5
PDCD7	-2.3	MGC21881	-2.4	CBX6	-2.5	SUMF2	-2.5
ZUFSP	-2.3	EWSR1	-2.4	SEC24C	-2.5	LEMD2	-2.5
CDHR3	-2.3	TMEM181	-2.4	WTAP	-2.5	A_24_P505255	-2.5
NOL6	-2.3	POM121	-2.4	HIST1H2BH	-2.5	A_24_P660797	-2.5
PIK3R3	-2.3	BTBD9	-2.4	ZDHHC14	-2.5	TMEM30A	-2.5
CD164	-2.3	A_32_P157671	-2.4	ZBTB9	-2.5	A_32_P233727	-2.5
ZBTB24	-2.4	MAGED1	-2.4	LARP1	-2.5	HGD	-2.5
LOC100507217	-2.4	LONRF1	-2.4	ZFAND2A	-2.5	NOXA1	-2.5
CRCP	-2.4	KANSL2	-2.4	C20orf3	-2.5	MLYCD	-2.5
GNA12	-2.4	IFNGR1	-2.4	RUNDC2C	-2.5	NECAP1	-2.5
UBTF	-2.4	A_24_P401381	-2.4	WBSCR16	-2.5	C8orf33	-2.5
YKT6	-2.4	EDEM3	-2.4	PVR	-2.5	GSN	-2.5
SH3BP5	-2.4	ACOT13	-2.4	TRIM26	-2.5	MTCH1	-2.5
SLCO5A1	-2.4	SLC12A2	-2.4	ASCC3	-2.5	RIOK1	-2.5
DNAJB2	-2.4	PTEN	-2.4	EWSR1	-2.5	EMID1	-2.5
KIAA1370	-2.4	ST7	-2.4	CEP41	-2.5	VPS26B	-2.5
DNAJB4	-2.4	GOLGA6L6	-2.4	RHBDD2	-2.5	LOC100506462	-2.5
ATP11C	-2.4	C13orf15	-2.4	EXT1	-2.5	TSPYL1	-2.5
CECR7	-2.4	C6orf89	-2.4	ALDOC	-2.5	GALNT6	-2.5
ABLIM1	-2.4	TMEM106B	-2.4	LOC100287482	-2.5	WDR82	-2.5
A_24_P499481	-2.4	SLC25A46	-2.4	AHCY	-2.5	PRKRIP1	-2.5
SPTBN1	-2.4	PHKA1	-2.4	TTC4	-2.5	A_24_P324644	-2.5
GTPBP5	-2.4	AY090769	-2.4	THC2678309	-2.5	KLHL35	-2.5
DSE	-2.4	PMS2L2	-2.4	BRD2	-2.5	ARID5B	-2.5
A_23_P22086	-2.4	NDUFB4	-2.4	EIF3F	-2.5	PON2	-2.6
LOC100132832	-2.4	IFI27L1	-2.4	P4HA2	-2.5	HIST1H2BL	-2.6
KIAA1370	-2.4	OPTN	-2.4	PMS2L2	-2.5	CLK2	-2.6
FBXL18	-2.4	CLK2	-2.4	A_32_P205139	-2.5	ENST00000445770	-2.6
ASB8	-2.4	UTP14A	-2.4	ZC3H6	-2.5	EMILIN3	-2.6
LONRF1	-2.4	AFG3L2	-2.4	FAM50B	-2.5	SLC2A13	-2.6
TMEM38B	-2.4	SSR1	-2.4	RAB24	-2.5	A_24_P341489	-2.6
HSPA8	-2.4	EPHA3	-2.4	BTG2	-2.5	DDIT3	-2.6
THC2610657	-2.4	GNL3L	-2.4	ZNF783	-2.5	SLC43A2	-2.6
RNF146	-2.4	REPS1	-2.4	DNAJB2	-2.5	SOCS6	-2.6
NID2	-2.4	CES2	-2.4	ECHDC2	-2.5	ABCF2	-2.6
TET2	-2.4	ZMIZ2	-2.4	SCAND3	-2.5	LOC339240	-2.6
ISY1	-2.4	RCN1	-2.4	TBCC	-2.5	A_24_P323916	-2.6

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
A_24_P178167	-2.6	TCP1	-2.7	CFLAR	-2.7	KDELR2	-2.8
THC2610134	-2.6	ZNF3	-2.7	A_24_P409697	-2.7	HIPK2	-2.8
STON1	-2.6	ACSS2	-2.7	TAOK3	-2.7	SYNM	-2.9
GET4	-2.6	GTF2I	-2.7	C6orf70	-2.7	SQSTM1	-2.9
A_24_P24806	-2.6	A_24_P290263	-2.7	CYCS	-2.7	FUCA1	-2.9
THC2565422	-2.6	UBE2E1	-2.7	CCDC142	-2.7	MAN2C1	-2.9
STOML1	-2.6	A_24_P392099	-2.7	ACTR5	-2.7	FOXO3	-2.9
ZNF79	-2.6	ARL17A	-2.7	ODZ3	-2.7	CDK5RAP3	-2.9
ZDHHC9	-2.6	PHF8	-2.7	NISCH	-2.7	MDH2	-2.9
HSPA6	-2.6	CASD1	-2.7	TMEM25	-2.7	ACTR3B	-2.9
STEAP1	-2.6	BU903025	-2.7	DDX56	-2.7	ZP3	-2.9
NEK9	-2.6	ENST00000331856	-2.7	PTEN	-2.7	FAM160B1	-2.9
UBXN8	-2.6	C6orf26	-2.7	KIAA1586	-2.8	A_24_P409471	-2.9
SLMO2	-2.6	TXLNA	-2.7	ENST00000448014	-2.8	C6orf225	-2.9
LOC100131564	-2.6	LOC100131564	-2.7	MUC3A	-2.8	TRIOBP	-2.9
BBS5	-2.6	DLEU2	-2.7	SRCRB4D	-2.8	FAM95B1	-2.9
ZC3H6	-2.6	ENST00000428471	-2.7	SLC22A5	-2.8	LOC283663	-2.9
TRIM68	-2.6	AK024382	-2.7	TMEM8B	-2.8	NEBL	-2.9
C15orf62	-2.6	LOC100133050	-2.7	A_24_P486503	-2.8	LOC220906	-2.9
FBN1	-2.6	ST7	-2.7	PEX1	-2.8	GRIN2C	-2.9
RGL1	-2.6	GTPBP4	-2.7	ATP8B3	-2.8	HOXB13	-2.9
CR616772	-2.6	NUS1	-2.7	FLJ45340	-2.8	C20orf177	-2.9
ENST00000434871	-2.6	ENST00000537552	-2.7	EME2	-2.8	HIPK2	-2.9
NMNAT1	-2.6	RPL27A	-2.7	ZNF433	-2.8	MAN2B2	-2.9
EWSR1	-2.6	ULK2	-2.7	A_23_P208582	-2.8	GCLM	-2.9
CECR5-AS1	-2.6	NPIP	-2.7	MALAT1	-2.8	RPL7L1	-2.9
DCAKD	-2.6	MMP11	-2.7	B4GALT1	-2.8	TRIM27	-2.9
HIST1H2BK	-2.6	PEX6	-2.7	CUL7	-2.8	FLJ45340	-2.9
UBTF	-2.6	PKIG	-2.7	RXRB	-2.8	TRAPPC6A	-2.9
A_24_P76210	-2.6	MALAT1	-2.7	C6orf168	-2.8	GNAS	-2.9
FKBP1B	-2.6	GJC2	-2.7	SULT2A1	-2.8	TJAP1	-2.9
LINGO2	-2.6	PDCD7	-2.7	CHPF2	-2.8	RASA4	-2.9
ANKRD11	-2.6	NUP98	-2.7	LOC100287482	-2.8	ZSCAN18	-2.9
NADK	-2.6	CNKSR3	-2.7	TMX4	-2.8	C6orf70	-2.9
NP414419	-2.6	ZFAND3	-2.7	PRMT5	-2.8	ARID1A	-3.0
COX19	-2.7	HCFC2	-2.7	FER1L4	-2.8	TTC17	-3.0
LOC388796	-2.7	NSF	-2.7	SSR4P1	-2.8	L07392	-3.0
SLC39A11	-2.7	GOSR1	-2.7	FXYD6	-2.8	POTEF	-3.0
A_24_P780609	-2.7	A_24_P636974	-2.7	CPT1A	-2.8	TBC1D25	-3.0
DLX6	-2.7	CTH	-2.7	MUC5B	-2.8	GUSBP4	-3.0
MBNL2	-2.7			LRRC41	-2.8	FLJ45340	-3.0

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
HDDC2	-3.0	PPM1J	-3.2	FAM168A	-3.4	KDELR2	-3.7
C13orf15	-3.0	RHOBTB3	-3.2	CD226	-3.5	BHLHE41	-3.7
MFGE8	-3.0	C6orf204	-3.2	AF257098	-3.5	ENST00000377186	-3.7
AK130366	-3.0	THC2713242	-3.2	LOC729852	-3.5	A_24_P238819	-3.7
GABARAPL3	-3.0	TMEM117	-3.2	AK021593	-3.5	A_32_P97798	-3.7
ENST00000435913	-3.0	ENST00000435913	-3.2	LOC100131053	-3.5	AEN	-3.7
DCLK1	-3.0	ENST00000399269	-3.2	C20orf177	-3.5	SLC12A2	-3.7
AFG3L1P	-3.0	SUV420H1	-3.2	FSTL1	-3.5	OLFM3	-3.7
MTMR11	-3.0	ZNF263	-3.2	CDK5RAP3	-3.5	ZNF462	-3.8
FAM71E1	-3.0	GLA	-3.2	AK090397	-3.5	MST1	-3.8
TLE2	-3.0	ZNF76	-3.2	GCLM	-3.5	AK092508	-3.8
FAM149A	-3.0	A_24_P859124	-3.2	CCR3	-3.5	NP450512	-3.8
FCGRT	-3.0	RPL13	-3.2	NDUFA10	-3.5	POLH	-3.8
AKAP9	-3.0	MIR22HG	-3.2	MIOS	-3.5	RBP1	-3.8
COL7A1	-3.0	CYCS	-3.3	ENST00000439362	-3.5	ENST00000360902	-3.8
A_24_P489649	-3.0	IFRD1	-3.3	RTDR1	-3.5	MAP2K6	-3.8
EIF4H	-3.0	PURB	-3.3	BX118285	-3.5	THC2677037	-3.9
ITPKB	-3.1	CPA5	-3.3	C7orf40	-3.5	BC029452	-3.9
GAS5	-3.1	VSTM2L	-3.3	SPTBN1	-3.6	C1orf53	-3.9
LRRC39	-3.1	SENP6	-3.3	BOC	-3.6	HEBP2	-3.9
A_24_P230466	-3.1	A_24_P298179	-3.3	A_32_P219704	-3.6	ENST00000553155	-3.9
KDELR2	-3.1	THC2744399	-3.3	ZNF441	-3.6	MIR1245A	-3.9
RBAK-LOC389458	-3.1	A_23_P28397	-3.3	EPM2AIP1	-3.6	THC2704459	-3.9
SRXN1	-3.1	IFRD1	-3.3	WNT10A	-3.6	THC2785860	-3.9
CDC42SE1	-3.1	ISL1	-3.3	BX537816	-3.6	SOLH	-3.9
CHPF2	-3.1	BRF2	-3.3	SLC3A1	-3.6	MYOM2	-3.9
FIGF	-3.1	ITFG2	-3.3	THC2748290	-3.6	KLHL14	-3.9
ZSCAN21	-3.1	THC2699065	-3.3	CU675788	-3.6	KCNQ2	-4.0
RSL1D1	-3.1	A_32_P31580	-3.3	PRKAB1	-3.6	THC2655842	-4.0
DMKN	-3.1	SIRT1	-3.4	LOC401431	-3.6	FAM82A1	-4.0
CREG1	-3.1	SPDYE8P	-3.4	FOSL1	-3.6	ENST00000433980	-4.0
COX19	-3.1	SLC22A18	-3.4	ZNF862	-3.6	LANCL2	-4.0
RIOK1	-3.1	RDM1	-3.4	CLYBL	-3.6	PTP4A1	-4.0
FTSJ2	-3.1	NDUFA10	-3.4	ZDHHC8P1	-3.6	BRD2	-4.0
ATP11C	-3.1	URGCP	-3.4	C6orf89	-3.6	BI836406	-4.0
ABCF2	-3.1	PTP4A1	-3.4	ENST00000416395	-3.6	UBR3	-4.0
BU929651	-3.1	ENST00000422603	-3.4	ENST00000456460	-3.6	C7orf50	-4.0
PRSS16	-3.1	RASSF8	-3.4	LINC00265	-3.6	TXNRD1	-4.0
POLM	-3.2	HIRA	-3.4	LRRC47	-3.7	ENST00000361201	-4.0
RNASET2	-3.2	A_24_P516728	-3.4	SENP6	-3.7		

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
CLN8	-4.0	TAC3	-4.3	EPHA3	-4.9	AKAP8L	-6.0
MCOLN2	-4.0	A_32_P145477	-4.3	SCHIP1	-5.0	ALDH1L1	-6.1
CDKN1A	-4.0	OTOA	-4.3	AGPHD1	-5.0	COL3A1	-6.1
THC2503819	-4.0	MST1P2	-4.3	PDE11A	-5.0	FABP7	-6.1
TMEM35	-4.0	CRCP	-4.4	PLEKHB1	-5.1	BCL2L11	-6.1
EEF1D	-4.0	ENST00000504184	-4.4	CASC2	-5.1	THC2544198	-6.2
CEP97	-4.0	RUFY2	-4.4	SESN1	-5.1	CDKN1A	-6.2
DTX3	-4.1	FAM169A	-4.4	FST	-5.1	B3GNT5	-6.2
A_23_P141785	-4.1	PTPRJ	-4.4	LOC100133091	-5.1	CEP97	-6.2
A_32_P149416	-4.1	ICAM4	-4.4	ELOVL4	-5.1	SOBP	-6.2
IGFBP4	-4.1	RASSF8	-4.4	DLK1	-5.2	BCHE	-6.2
TTC39A	-4.1	PLCH1	-4.4	LOC100505938	-5.2	LRRC17	-6.3
FAM82A1	-4.1	PAPSS2	-4.4	RASSF8	-5.2	C4orf34	-6.3
RNASET2	-4.1	PAX4	-4.5	FZD1	-5.2	NKX2-5	-6.4
AK7	-4.1	KGFLP1	-4.5	CCDC3	-5.2	BAALC	-6.4
USP6	-4.1	GPCPD1	-4.5	CNTNAP2	-5.2	PBX1	-6.4
B4GALT1	-4.1	ASPRV1	-4.6	NR2F2	-5.2	SAT1	-6.5
IGLL1	-4.1	AK124097	-4.6	AI698357	-5.3	SERPINB1	-6.6
ATP1B2	-4.1	TRIM4	-4.6	ISOC1	-5.3	CA13	-6.6
IRS1	-4.1	HES2	-4.6	SLC16A9	-5.3	HLA-DMA	-6.6
BQ674642	-4.2	CD247	-4.6	AK021570	-5.4	ENST00000521369	-6.6
PAPSS2	-4.2	C12orf68	-4.6	COL20A1	-5.4	FNDC4	-6.7
FAM169A	-4.2	GABARAPL1	-4.6	PRKAR2B	-5.4	NEGR1	-6.7
RASD2	-4.2	STOX2	-4.7	WNT5B	-5.4	PLVAP	-6.8
CITED1	-4.2	BC037328	-4.7	MIRLET7BHG	-5.4	CAST	-6.8
GAD1	-4.2	CSRP2	-4.7	MAFIP	-5.4	ME1	-6.8
CRYL1	-4.2	FBLN2	-4.7	MGC16121	-5.4	SAT1	-6.9
HLA-DMB	-4.2	TDRD10	-4.8	SLC27A6	-5.5	SC5DL	-6.9
C9orf167	-4.2	A_24_P409182	-4.8	MYCBPAP	-5.5	PPP1R3D	-6.9
PHF14	-4.2	HLA-DMA	-4.8	NFYA	-5.6	AK026965	-7.0
ANKRD20A2	-4.2	GNAS	-4.8	GNAS	-5.6	SNX7	-7.1
COL3A1	-4.2	AL834280	-4.8	A_32_P230537	-5.6	RTTN	-7.1
DYNLT3	-4.2	SESN1	-4.8	C6orf48	-5.6	HMOX1	-7.1
BC016022	-4.2	HSD17B8	-4.8	CAST	-5.6	GPC3	-7.1
GNAZ	-4.3	ADAMTS19	-4.9	OXR1	-5.6	SYCP3	-7.1
FGF7	-4.3	LDHD	-4.9	A_23_P108534	-5.7	FOXN4	-7.2
OSGIN1	-4.3	BTG1	-4.9	KCNJ14	-5.7	PTPRJ	-7.2
A_24_P935852	-4.3	ENST00000479981	-4.9	COL2A1	-5.7	ANG	-7.2
DSCR6	-4.3	CPXM1	-4.9	A_32_P41594	-5.7	BEGAIN	-7.2
A_24_P587993	-4.3	SULT2A1	-4.9	PTGFRN	-5.7	EIF3F	-7.2
BC001335	-4.3			RGS11	-5.9	ME1	-7.3

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
NR2F2	-7.3	GPC4	-8.9	MCF2	-12.4	HYLS1	-19.4
THC2686110	-7.4	TP53TG1	-9.0	AF100640	-12.4	CROT	-19.7
FAM5C	-7.4	TNFRSF10D	-9.1	A_23_P139166	-12.4	EPHX2	-19.8
IGF1R	-7.5	IFI27L2	-9.2	PDE6H	-12.5	AF264621	-19.9
PFKFB3	-7.5	PLA2G2F	-9.2	EPCAM	-12.6	HTATIP2	-20.0
MGP	-7.5	METTL7A	-9.3	MYLIP	-12.6	DNAJC12	-20.1
PITX1	-7.6	A_32_P72541	-9.4	A_24_P401521	-12.8	ANKRD20A2	-20.3
CR936711	-7.6	CHRNA3	-9.5	FBXO8	-13.0	GAD1	-20.7
ME1	-7.6	CNTNAP3B	-9.5	EFHC2	-13.0	FBN2	-20.8
RERG	-7.6	GLIS1	-9.5	L3MBTL3	-13.4	PPP4R4	-21.0
MIR137HG	-7.6	ATP1B1	-9.5	TLE1	-13.4	CDCA7L	-21.5
THC2512148	-7.8	PDE3A	-9.5	LOC100505806	-13.5	GLCCI1	-21.7
FGL1	-7.8	AB014766	-9.7	A_24_P597242	-13.8	PTPRK	-21.7
COL3A1	-7.8	GCH1	-9.7	A_24_P910080	-14.0	AY227436	-21.9
SC5DL	-7.8	PPP4R4	-9.7	CNTN1	-14.1	CDH2	-22.0
STAMBPL1	-7.8	FGF7	-9.8	CTNNA3	-14.1	ARHGDIB	-22.2
HAND2	-7.9	RIN2	-10.1	SCIN	-14.2	HAPLN1	-22.4
ACTA2	-7.9	CYB5R2	-10.1	TFPI	-14.2	GAD1	-22.5
JAKMIP3	-8.0	ATP1B1	-10.3	MAL2	-14.4	CELF2	-22.5
DHDH	-8.0	SLC16A14	-10.3	A_24_P920715	-14.4	C8orf4	-22.7
CITED2	-8.0	ZP3	-10.4	RBM20	-15.4	ANKRD20A2	-22.7
CNTNAP3	-8.0	CAMK4	-10.5	CNTNAP3B	-15.4	MDK	-22.9
ANKRD22	-8.1	TNFRSF11B	-10.5	THC2682885	-15.6	IGF1R	-23.1
CTSF	-8.1	ENST00000462693	-10.6	PRINS	-15.7	MPPED2	-23.2
METTL7A	-8.2	ATP10A	-10.7	LOC100132593	-15.7	PDE11A	-23.4
LOC90499	-8.2	ENST00000514673	-10.7	SFRP1	-15.8	CGREF1	-23.8
RGS20	-8.3	FAS	-10.9	EFNB2	-15.9	SGCE	-23.8
LOC157627	-8.3	ENST00000318245	-10.9	LMO4	-16.0	EPHB6	-23.8
KIAA1751	-8.3	SESN3	-10.9	SYNE1	-16.1	SLC16A14	-24.0
C8orf85	-8.4	ICA1	-10.9	MYO3B	-16.2	PDZRN4	-24.2
P2RX5	-8.4	MMRN1	-11.0	CARD18	-16.3	LUM	-24.2
LOC284561	-8.4	SP5	-11.0	KRT80	-16.4	BF217859	-24.6
ZDBF2	-8.6	PRAMEF8	-11.1	FAM46A	-16.4	PAX6	-24.9
TMCO4	-8.6	THC2661509	-11.2	KANK1	-17.1	RARB	-25.3
TP53TG1	-8.6	FERMT1	-11.3	THC2646628	-17.3	SEMA5A	-25.4
RHOH	-8.6	L3MBTL3	-11.4	THC2644897	-17.7	CYB5A	-25.5
IDO1	-8.7	NFIA	-11.6	GSTO2	-17.8	GLCCI1	-25.6
PLAC1	-8.7	FUT4	-11.8	CHODL	-18.0	HTATIP2	-25.7
RBM47	-8.7	CLIP4	-12.2	SLITRK1	-18.0	THC2535223	-25.8
SLC38A5	-8.8	NDP	-12.4	TFPI	-18.4	TMPRSS15	-25.9
CEP44	-8.8			ATRNL1	-19.4	ITGA1	-26.5

Appendix V Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
TOX	-26.6	CHRNA9	-77.0				
ABCB1	-27.2	MAOB	-83.4				
RERGL	-27.3	ABCB4	-131.0				
KANK1	-27.8	BEX1	-138.0				
PLAC8	-28.5	ANXA1	-208.2				
DOK6	-28.5	PCDH20	-252.7				
EDIL3	-28.6	ANXA10	-285.9				
SLITRK1	-28.7						
MLH1	-30.1						
PEG10	-30.4						
SORBS2	-30.4						
ABCA5	-31.8						
THC2712710	-31.9						
AGTR1	-32.5						
SNTG1	-32.8						
LUM	-34.1						
DLC1	-36.7						
TMEFF2	-38.1						
C4orf49	-38.2						
GPM6B	-39.8						
NTS	-40.2						
ALDH1A1	-41.5						
HECA	-42.2						
RUNDC3B	-42.3						
KIAA1217	-42.3						
FAM198B	-43.5						
ASB9	-46.2						
DCDC5	-46.8						
DLC1	-47.4						
DMRT3	-50.7						
BEX2	-53.8						
STXBP5L	-54.2						
AK094603	-54.4						
LRP1B	-59.5						
DCN	-61.9						
MGAT4C	-65.8						
SPP1	-69.1						
SLITRK6	-72.0						
VGLL3	-72.9						
RASSF9	-73.3						
KCNK10	-73.7						

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
FOXP1	382	TGFB2	13.7	CD302	8.0	POU3F1	6.4
FOXP1	148	SOX6	13.7	HOXA10	7.8	AUTS2	6.4
RBMS3	101	DUSP6	13.5	GPR27	7.8	RIPPLY2	6.3
OTP	77.2	SLC39A8	13.3	CDH11	7.7	GSTT2	6.3
HOXD10	75.0	SP7	12.7	FOXD1	7.7	NRXN1	6.3
HS3ST3B1	43.8	THC2610890	12.7	NRIP1	7.6	LOC375295	6.2
PRR16	37.9	PDGFRB	12.4	CYR61	7.6	ATXN3	6.2
SEMA3D	33.2	CYR61	12.0	FLRT2	7.6	HOXD3	6.1
HS3ST3A1	30.9	RSPO3	12.0	MRAP2	7.5	HMMR	6.0
S1PR1	28.9	ESRRG	11.8	ZNF826P	7.4	CYP1B1	6.0
PDGFRA	27.2	ENST00000323496	11.6	GRB14	7.4	DZANK1	5.9
HOXD11	26.1	ENST00000428809	11.5	ANO3	7.3	CCDC102B	5.9
RBMS3	23.3	CBR3	10.9	THC2704911	7.2	C18orf56	5.9
GRIA3	21.3	ODZ2	10.9	SETBP1	7.2	DOK7	5.9
TMSB4X	20.2	GPR126	10.7	FST	7.1	FAM122C	5.9
TMTC1	19.9	MARCKS	10.5	TMEM100	7.1	NCAM2	5.8
SULF1	19.7	CALCA	10.0	KLF8	7.1	FABP7	5.8
MMP10	18.9	THC2732175	9.8	SOX9	7.0	BC015334	5.8
SPARCL1	18.4	COL1A2	9.7	C1orf173	7.0	THC2553406	5.8
OVOL2	18.4	FOXP2	9.6	INPP4B	7.0	AGPAT4	5.7
TMSB4X	18.2	GDNF	9.6	HOXB6	7.0	CA2	5.7
PDZRN3	18.0	CDH7	9.5	SOX2	7.0	HEY1	5.7
BX092137	17.8	EIF4E3	9.5	ENST00000520259	6.9	CCDC34	5.7
C7orf58	17.6	X15674	9.4	PTGER2	6.9	ATP6V0D2	5.7
TACSTD2	17.5	DPYSL2	9.4	KANK4	6.9	IRX5	5.7
SETBP1	17.1	NEFL	9.4	PRTFDC1	6.8	CCDC102B	5.6
C1orf172	16.5	GUCY1B3	9.4	SEMA6D	6.8	SHISA3	5.5
AKAP5	15.7	CRNDE	9.3	PRR11	6.8	AKR1C3	5.5
LHX2	15.7	MBNL3	9.3	TMSB4X	6.8	ENST00000505709	5.5
LOX	15.6	TMTC1	9.2	MTL5	6.8	CENPK	5.5
TMTC1	15.5	CBR1	9.2	MAP1B	6.8	PPP1R1C	5.5
GCG	15.0	CYP4X1	9.2	TMC7	6.8	JUN	5.4
CALCA	14.9	ETV1	9.1	BPNT1	6.8	AMOT	5.4
PPP4R4	14.8	ATP6V0D2	9.0	HHIP	6.7	MBOAT1	5.4
SFTA1P	14.6	DPYSL2	9.0	GUCY1A3	6.7	PAQR8	5.4
GRM8	14.6	ATRNL1	8.9	ANKRD45	6.7	GSTM4	5.4
ENST00000456585	14.0	C7orf58	8.5	MMP3	6.7	LOC439911	5.3
IRX5	13.9	ENST00000537149	8.2	SAMD13	6.6	SPC25	5.3
VAV3	13.9	SGCG	8.1	UTRN	6.6	STMN3	5.3
GNG11	13.8	THC2753543	8.1	MAP1B	6.5	DFNB31	5.2
CBR3	13.7	EYA4	8.0	PCDHB5	6.4	DHFR	5.2

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
MNS1	5.2	LOC100144602	4.6	PCDHB14	4.2	LOC100505566	3.8
PDGFC	5.2	BC032755	4.6	C8orf83	4.2	SMPDL3A	3.8
SEMA3A	5.2	GJA1	4.6	CDK19	4.2	VSIG10	3.8
PTX3	5.2	BDH2	4.6	DUSP19	4.2	C12orf48	3.8
LOC100506421	5.1	LOC100505695	4.5	BRWD3	4.2	GSTT2	3.8
MIS18BP1	5.1	DEPDC1B	4.5	BM690036	4.2	IVNS1ABP	3.8
RPS6KA6	5.1	GSTM4	4.5	ZEB2	4.2	CDK14	3.8
VCX2	5.1	HOXD8	4.5	NCAPG2	4.2	RAB27A	3.7
GPM6A	5.1	ENC1	4.5	OTUD4	4.2	THC2628387	3.7
DZANK1	5.1	THC2638839	4.5	LOC100507312	4.1	LOC100506268	3.7
THC2538534	5.1	CD302	4.5	HIST1H4L	4.1	ETV1	3.7
MTL5	5.1	CDK14	4.5	SWAP70	4.1	TSPAN12	3.7
KIF16B	5.1	FLRT2	4.5	VCX	4.1	RBBP9	3.7
AK125162	5.1	HS6ST2	4.5	FZD1	4.1	KIAA1009	3.7
TEKT4P2	5.1	GPR126	4.5	LOC100287628	4.1	SGTB	3.7
ERI2	5.0	TNNI3K	4.4	GRIA3	4.1	PDCL	3.7
LOC100131289	5.0	PPP2R2B	4.4	C7orf55	4.1	STK33	3.7
WDHD1	5.0	THC2575678	4.4	SGOL1	4.1	CORO2A	3.7
NRXN1	5.0	LIN28A	4.4	LRRIQ1	4.0	FGF9	3.7
EIF4E3	5.0	AK129542	4.4	KIF14	4.0	NAALAD2	3.7
CALN1	4.9	FRMD4A	4.4	CBX3P2	4.0	CNTLN	3.7
C20orf103	4.9	ENST00000555442	4.4	INADL	4.0	KLF8	3.7
GFRA2	4.8	TMSB15B	4.4	TYRP1	4.0	CA427179	3.6
ACBD5	4.8	COL17A1	4.4	RB1	4.0	ECHDC2	3.6
ZNF273	4.8	NRXN1	4.4	KIF1B	4.0	TRPM6	3.6
MBD2	4.8	RTKN2	4.4	HIST1H4D	3.9	HIST1H4C	3.6
ANXA2	4.8	MIS18BP1	4.4	ERBB4	3.9	RFTN2	3.6
C9orf150	4.8	NCAM2	4.4	ZNF618	3.9	C12orf48	3.6
AS3MT	4.8	DDAH1	4.4	C21orf58	3.9	ZC4H2	3.6
RSPO2	4.8	KCNMA1	4.3	KIAA1009	3.9	GPM6B	3.6
BCAS4	4.8	BUB1	4.3	LMF1	3.9	LOC727869	3.6
THC2524341	4.8	LOC100506268	4.3	CASC5	3.9	RCOR3	3.6
TFPI2	4.8	CTNNA2	4.3	HOXB4	3.9	DEPDC4	3.6
TRIB2	4.8	CDC25C	4.3	MMP1	3.8	KIAA0586	3.6
PPP4R4	4.7	THC2656519	4.3	VCX3A	3.8	HOXD9	3.5
RFC3	4.7	CSRNP3	4.3	PDE1A	3.8	IDO2	3.5
CELF2	4.7	SLC45A3	4.3	FRRS1	3.8	DMRT1	3.5
GAB1	4.7	RCAN3	4.2	GTF2A1	3.8	THC2638025	3.5
FAM161A	4.7	LINC00470	4.2	ENST00000460407	3.8	NAP1L1	3.5
EPHA5	4.6	HOXB5	4.2	PHF15	3.8	PBX1	3.5
KLHDC9	4.6	CENPI	4.2	SCN9A	3.8	C9orf100	3.5

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
THC2703681	3.5	DOCK4	3.4	STK39	3.2	AK075186	3.1
THC2648509	3.5	EPB41	3.4	RADIL	3.2	C8orf83	3.1
PCDH18	3.5	MMS22L	3.4	MIR210HG	3.2	CAMKMT	3.0
BG695979	3.5	LMO1	3.4	MME	3.2	RCAN3	3.0
THC2552705	3.5	ATXN3	3.4	ZNF273	3.2	KIAA0430	3.0
AP1M2	3.5	NEFL	3.4	DNMT3B	3.2	TMEM159	3.0
DLGAP5	3.5	SLC30A5	3.3	C18orf54	3.2	FANCL	3.0
ARL6IP6	3.5	PBX1	3.3	IRX3	3.2	STAU2	3.0
STAU2	3.5	MOB3B	3.3	TTC7A	3.2	C6orf162	3.0
AF034187	3.5	NUF2	3.3	CEP112	3.2	ALS2CR8	3.0
FAM63A	3.5	EIF2C4	3.3	MYLK	3.2	SATB2	3.0
RAB3D	3.5	THC2756939	3.3	APAF1	3.2	TMOD3	3.0
GSTM4	3.5	SMAD9	3.3	KIF11	3.2	BORA	3.0
OMA1	3.4	DIRAS3	3.3	KIF1B	3.2	HIST1H2BD	3.0
IRS2	3.4	TUBB2B	3.3	KIAA1147	3.2	THC2537856	3.0
BRCA1	3.4	LRRC20	3.3	NTF4	3.2	ENST00000432751	3.0
NDC80	3.4	CCNB2	3.3	OMA1	3.2	HSD17B11	3.0
C6orf164	3.4	THC2666403	3.3	DOCK4	3.2	MLLT3	3.0
THC2563460	3.4	AK024926	3.3	BQ881683	3.2	SLC12A6	3.0
DENND5B	3.4	MBD5	3.3	CEP57L1	3.1	ENST00000451759	3.0
LOC440288	3.4	SRP9	3.3	SIPA1	3.1	ZNF789	3.0
GNG2	3.4	DARS2	3.3	TTK	3.1	IFT81	3.0
RMI2	3.4	HIST1H4B	3.3	TBC1D1	3.1	MCM3AP-AS1	3.0
KIAA1841	3.4	FAM161A	3.3	ZNF367	3.1	P2RY1	3.0
STON1	3.4	THC2616195	3.3	CYR61	3.1	NDNF	3.0
NUDT7	3.4	GEM	3.3	ZNF876P	3.1	ATRNL1	3.0
BQ933774	3.4	SPICE1	3.3	BX389966	3.1	LOC100128822	3.0
NDE1	3.4	HSD17B11	3.3	LOC100505616	3.1	GRASP	3.0
QKI	3.4	PHIP	3.3	ASPM	3.1	DIAPH3	3.0
AK054718	3.4	ST7-AS1	3.3	CORO2A	3.1	PCDHA11	3.0
TES	3.4	THC2689749	3.3	C6orf112	3.1	ENST00000514048	3.0
AK128413	3.4	TLE4	3.3	C9orf86	3.1	METTL7A	3.0
RBM4	3.4	ABCA1	3.3	RBL1	3.1	METTL7A	3.0
PRPH2	3.4	FSD1L	3.3	ASPM	3.1	BC014971	2.9
HIST2H2AC	3.4	IL28RA	3.3	SNAI2	3.1	STK17A	2.9
MAGI2	3.4	IFT80	3.2	FANCI	3.1	GSTM1	2.9
LRRFIP1	3.4	PIF1	3.2	KIAA0586	3.1	PRCP	2.9
PCMTD1	3.4	ENST00000456688	3.2	THC2679424	3.1	TTC8	2.9
SPATA6	3.4	MLIP	3.2	ABCA10	3.1	CDS1	2.9
ENST00000428928	3.4	ANXA2	3.2	OXCT1	3.1	MDFI	2.9
LOC440434	3.4	WIF1	3.2	MLF1IP	3.1	SLC6A6	2.9

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
CARD8	2.9	SLC38A9	2.8	C16orf55	2.7	TLE4	2.7
MME	2.9	KNTC1	2.8	LOC100507568	2.7	PFKFB4	2.7
RBM43	2.9	CBX1	2.8	GEMIN8P4	2.7	TMEM187	2.7
OCA2	2.9	RWDD3	2.8	HNRNPA3	2.7	LYRM7	2.7
TCF7L1	2.9	GRRP1	2.8	KIAA1958	2.7	ACN9	2.7
LOC375295	2.9	C20orf201	2.8	STK17A	2.7	C9orf95	2.7
STK17B	2.9	TRIM5	2.8	CDC42EP3	2.7	DNASE1L1	2.7
BC000986	2.9	POLA1	2.8	CR599799	2.7	PARVA	2.7
C14orf167	2.9	RSPO2	2.8	HIST1H4E	2.7	PLK4	2.7
SPON2	2.9	C14orf28	2.8	U88048	2.7	SEC62	2.7
RPRML	2.9	ENST00000557691	2.8	RFFL	2.7	DEPDC1	2.7
ABCC6	2.9	PDE7A	2.8	NIPSNAP3B	2.7	LMBR1	2.7
BC018626	2.9	ACTL8	2.8	PUS7L	2.7	KIAA1704	2.7
THC2756581	2.9	AB593167	2.8	GNB4	2.7	NR3C1	2.7
ANKRD43	2.9	EXTL2	2.8	GSTCD	2.7	PCMTD2	2.7
EPHA5	2.9	DIAPH3	2.8	TUBB8	2.7	GNAI3	2.7
STK39	2.9	RBM20	2.8	BOD1L	2.7	DEPDC7	2.7
CENPC1	2.9	WBP5	2.8	C12orf47	2.7	TCFL5	2.7
MYO1B	2.9	ABCD3	2.8	ZBTB8A	2.7	CREBL2	2.7
DDX46	2.9	NHLRC2	2.8	KIAA1841	2.7	DISC1	2.7
CR594811	2.9	PBK	2.8	C14orf109	2.7	ATXN3	2.6
B3GALTL	2.9	BC048213	2.8	LOC730101	2.7	CD2AP	2.6
SPICE1	2.9	GLRX	2.8	AK056771	2.7	PRIM2	2.6
C1GALT1	2.9	NUDT11	2.8	ICK	2.7	CD247	2.6
PDE1A	2.9	THC2596442	2.8	SATB1	2.7	RBMS3	2.6
BTBD8	2.9	EIF2C4	2.8	OIP5	2.7	C14orf142	2.6
VEGFC	2.9	SLC25A40	2.8	KIAA1524	2.7	RACGAP1	2.6
DLG3	2.9	C9orf40	2.8	THC2723931	2.7	FLJ42709	2.6
THC2717828	2.9	C6orf170	2.8	ABCA11P	2.7	TMEM107	2.6
AGL	2.9	TRPA1	2.8	KLHDC2	2.7	CR598370	2.6
C17orf104	2.9	MTBP	2.8	ACOT11	2.7	NT5DC1	2.6
IGFLR1	2.9	CDC45	2.8	SLC25A40	2.7	ASB2	2.6
C1orf112	2.9	IFIT1	2.8	PRSS30P	2.7	DLG3	2.6
C21orf119	2.9	KIF20B	2.8	CENPW	2.7	WWOX	2.6
CAPS2	2.9	AK023629	2.8	MMS19	2.7	PJA2	2.6
NDC80	2.9	TCF4	2.8	LOC100507599	2.7	ARL6IP5	2.6
PCMTD1	2.9	SNHG10	2.8	ANXA2P3	2.7	HIP1	2.6
RAB3D	2.9	PRIM2	2.8	THC2646608	2.7	C10orf140	2.6
C5	2.9	MCART1	2.8	ZNF618	2.7	SLC10A4	2.6
CKLF	2.8	LOC100506831	2.8	PCDHB9	2.7	LOC100130890	2.6
UGP2	2.8	ACYP1	2.8	MMD	2.7	MTAP	2.6

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SEMA3A	2.6	ZRANB3	2.6	ANXA2P1	2.5	GU228580	2.4
CDCA2	2.6	XM_929965	2.6	PTPN12	2.5	KIF18A	2.4
CHD6	2.6	NIPSNAP3A	2.6	NDE1	2.5	CIT	2.4
LIMD2	2.6	FBXO16	2.6	LOC100652849	2.5	DPY19L4	2.4
VCAN	2.6	LOH12CR2	2.6	NUB1	2.5	SIRT3	2.4
BDH2	2.6	C6orf165	2.6	CR936711	2.5	ZCRB1	2.4
SRGAP2P1	2.6	CCDC74B	2.6	AI928490	2.5	CHRNB1	2.4
LOC100506233	2.6	GPER	2.6	CLASP2	2.5	KIAA1958	2.4
TBX15	2.6	NT5DC1	2.6	GMIP	2.5	MCCC1	2.4
U2AF1	2.6	PALM3	2.5	FAM43B	2.5	FRMD6	2.4
PDCL	2.6	LOC100507316	2.5	NUDT6	2.5	C1orf38	2.4
TMEM60	2.6	HNRNPA3	2.5	NEK2	2.5	FAM115A	2.4
MMS22L	2.6	ADD3	2.5	ALMS1	2.5	NEK2	2.4
TUBB3	2.6	THC2655194	2.5	DNAH14	2.5	NUSAP1	2.4
TTC7A	2.6	HPS1	2.5	ZNF138	2.5	CA8	2.4
SGOL2	2.6	GLI1	2.5	ZNF33A	2.5	ESCO2	2.4
GPSM2	2.6	SPIN4	2.5	DISP2	2.5	CCDC74B	2.4
PLAT	2.6	MBTD1	2.5	BC000986	2.5	ECT2	2.4
RAB27A	2.6	BC019907	2.5	TTC33	2.5	ZNF37BP	2.4
RND3	2.6	BLM	2.5	FGF5	2.5	SMC2	2.4
C2orf68	2.6	THC2560357	2.5	SPATA6	2.5	FAM175A	2.4
PAIP2	2.6	TBC1D8	2.5	SNHG13	2.5	DLK1	2.4
FRZB	2.6	ENST00000395427	2.5	RP2	2.5	ITGB3BP	2.4
HDX	2.6	MSH2	2.5	GREB1	2.5	ARNT	2.4
RABGAP1L	2.6	B3GALTL	2.5	SS18L2	2.5	RAD51AP1	2.4
CDC42BPG	2.6	MOSPD2	2.5	XPNPEP3	2.5	RIC3	2.4
PDE1A	2.6	PRIM1	2.5	MND1	2.5	LINC00470	2.4
MLLT3	2.6	PHLDB1	2.5	TMTC4	2.5	KIF20A	2.4
SWAP70	2.6	CASP10	2.5	SPC24	2.5	KANK2	2.4
LOC100288911	2.6	SPAG5	2.5	BF514006	2.5	METTL21A	2.4
HIP1	2.6	ZBTB1	2.5	WBP4	2.5	THC2505678	2.4
TIFA	2.6	MGAT3	2.5	C12orf47	2.5	TIGD7	2.4
GAS8	2.6	PRSS35	2.5	ERBB2	2.5	ACVR2B	2.4
RIMKLB	2.6	CD200	2.5	DCK	2.5	THC2746571	2.4
STMN1	2.6	KIAA0101	2.5	WDHD1	2.5	AK027667	2.4
RIN2	2.6	UNC5CL	2.5	LPAR3	2.5	PCDHB16	2.4
GAB1	2.6	LOC100270746	2.5	LOC646719	2.4	ANXA2	2.4
THC2729899	2.6	ITSN1	2.5	C1orf190	2.4	C14orf33	2.4
ENST00000432961	2.6	CMIP	2.5	CENPW	2.4	NIN	2.4
DHFR	2.6	ADCY7	2.5	LOC644246	2.4	RFC1	2.4
C7orf31	2.6	CENPF	2.5	CENPF	2.4	DIAPH3	2.4

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
NDUFA5	2.4	AGBL2	2.4	C4orf3	2.3	MST4	2.3
MDH1B	2.4	HFE	2.4	ALG13	2.3	C7orf23	2.3
HIST1H4K	2.4	CEP128	2.4	CFLAR	2.3	LOC400043	2.3
AK054902	2.4	CREB3L4	2.4	SRSF12	2.3	RIMS3	2.3
CEP55	2.4	PIGZ	2.3	CTNND1	2.3	FAM54A	2.3
NUCKS1	2.4	BRCA2	2.3	MASTL	2.3	CCDC88A	2.3
FAM175A	2.4	SLC7A8	2.3	ERN1	2.3	MYB	2.3
ROM1	2.4	BTNL2	2.3	UFL1	2.3	CSTF3	2.3
SIRT3	2.4	C1GALT1	2.3	CBX7	2.3	BBS5	2.3
SIPA1L3	2.4	CCNA2	2.3	LRRC37A4	2.3	DNMT3A	2.3
C7orf73	2.4	RBPMS	2.3	THC2695815	2.3	CARD6	2.3
MIS18A	2.4	C2orf68	2.3	MEX3A	2.3	METTL21A	2.3
SPINK4	2.4	BX648207	2.3	STK17B	2.3	C5orf56	2.3
RASIP1	2.4	SENP7	2.3	ANO8	2.3	MAP2K6	2.3
RUNX2	2.4	CDH24	2.3	C5orf44	2.3	LSM3	2.3
MELK	2.4	MLH1	2.3	NDRG3	2.3	SCAMP1	2.3
SUMO3	2.4	ICMT	2.3	KLRG1	2.3	WDFY2	2.3
C5orf13	2.4	HIST1H1D	2.3	WDR25	2.3	THC2648759	2.3
RSPO3	2.4	LXN	2.3	LOC285141	2.3	PIK3C2G	2.3
CCDC111	2.4	C10orf95	2.3	LRRC40	2.3	LCORL	2.3
BC141946	2.4	THC2672257	2.3	RILP	2.3	CCNT2	2.3
AK093429	2.4	SUV39H2	2.3	DPYD	2.3	TARDBP	2.3
IFT88	2.4	SMCHD1	2.3	MORC2	2.3	LYRM7	2.3
CRYZ	2.4	CDCA7	2.3	PDE1A	2.3	SPRYD4	2.3
LACTB2	2.4	RACGAP1	2.3	RRM1	2.3	LOC145783	2.3
ARHGAP11A	2.4	MYSM1	2.3	NEIL3	2.3	ARL5B	2.3
HRSP12	2.4	CR599788	2.3	ETS2	2.3	ZAK	2.3
DZANK1	2.4	IVNS1ABP	2.3	THC2507829	2.3	NCAPH	2.2
RGS13	2.4	BRIP1	2.3	SFR1	2.3	BNIP3L	2.2
AK022793	2.4	L1TD1	2.3	ENAH	2.3	THC2519126	2.2
VSIG10L	2.4	TRIM14	2.3	CAND2	2.3	CENPP	2.2
IL11	2.4	KATNAL1	2.3	HNRNPA3	2.3	GLYATL1	2.2
HAUS6	2.4	CU686711	2.3	MRE11A	2.3	C8orf51	2.2
PEX13	2.4	POLE2	2.3	MMS22L	2.3	ATAD2	2.2
RUNX2	2.4	SV2A	2.3	CCDC88A	2.3	THC2752681	2.2
IQGAP2	2.4	GYG2	2.3	KLF15	2.3	FCHO2	2.2
C3orf18	2.4	LRTOMT	2.3	CSPG4	2.3	HIST1H3B	2.2
TDP1	2.4	BG612665	2.3	CD109	2.3	TRUB1	2.2
PHF15	2.4	E2F8	2.3	SAP130	2.3	ARL5B	2.2
ADC	2.4	PI4K2B	2.3	AK026195	2.3	TOX	2.2
HIST1H1E	2.4	THC2684461	2.3	TNFSF4	2.3	CXXC4	2.2

Appendix VI Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
TTC39A	2.2	CRY1	2.2	ANKRD36	2.2	ANP32E	2.2
GSTM5	2.2	LOC645676	2.2	HOXB9	2.2	ARMC9	2.2
KLHDC3	2.2	BMF	2.2	FAM189B	2.2	HNRNPA3	2.2
GPR19	2.2	HAUS5	2.2	C7orf11	2.2	PHF21B	2.2
C4orf46	2.2	SPECC1	2.2	TOX	2.2	C12orf69	2.2
THC2603239	2.2	GNB4	2.2	MSX1	2.2	FLJ42709	2.2
NINL	2.2	FBXO3	2.2	EIF4EBP2	2.2	WDFY3-AS2	2.2
ANGPTL2	2.2	PIGC	2.2	SNX5	2.2	KRT222	2.2
MZT1	2.2	PARD6G	2.2	WIPI2	2.2	SENP7	2.2
ADD3	2.2	TRERF1	2.2	NUDT21	2.2	TMEM169	2.2
MDGA1	2.2	BAG4	2.2	STMN3	2.2	HADH	2.1
NTNG1	2.2	RSU1	2.2	RNF152	2.2	PPP1R35	2.1
LOC645722	2.2	FAM178A	2.2	LOC642236	2.2	HMGB1	2.1
C4orf21	2.2	THC2536817	2.2	BTN2A2	2.2	TMC6	2.1
INCENP	2.2	SKIL	2.2	BLVRA	2.2	DHFR	2.1
RCBTB1	2.2	ZFYVE16	2.2	BPNT1	2.2	CEP57L1	2.1
FANCD2	2.2	ENST00000557373	2.2	LOC100289361	2.2	DZIP1L	2.1
MAP2K6	2.2	HIST2H2AB	2.2	C11orf71	2.2	TRIM37	2.1
MRI1	2.2	ZDHHC24	2.2	PARP11	2.2	ZDHHC20	2.1
C6orf165	2.2	CTAGE1	2.2	KIF16B	2.2	DICER1-AS	2.1
SGOL1	2.2	THC2622100	2.2	PIAS4	2.2	RPL13P5	2.1
CTNNBIP1	2.2	MEG3	2.2	PVRL2	2.2	FDX1	2.1
BX107836	2.2	GTF2IRD1	2.2	MPZL3	2.2	F2R	2.1
OSBPL1A	2.2	UHRF1	2.2	HGF	2.2	C6orf211	2.1
LINC00470	2.2	OGG1	2.2	POFUT1	2.2	TIA1	2.1
CENPE	2.2	CTDSPL2	2.2	MCEE	2.2	EMP2	2.1
CU692129	2.2	BCLAF1	2.2	C4orf27	2.2	FLVCR1-AS1	2.1
THC2537179	2.2	PHTF1	2.2	AZI1	2.2	TMEM55A	2.1
C6orf162	2.2	CDCA7	2.2	AK125351	2.2	DLG5	2.1
NCAPG	2.2	C14orf93	2.2	SNRNP35	2.2	KLHDC3	2.1
PJA1	2.2	BMPER	2.2	CPPED1	2.2	DMC1	2.1
PSRC1	2.2	CASP6	2.2	POLD3	2.2	BG216262	2.1
DAZAP1	2.2	NOTCH4	2.2	ANKRD44	2.2	ARHGAP11A	2.1
PGM3	2.2	CRYZ	2.2	PHC1	2.2	TMPO	2.1
H1FX	2.2	BIVM	2.2	LOC728705	2.2	THC2538568	2.1
TBXA2R	2.2	C10orf76	2.2	LOC728392	2.2	CU675788	2.1
FANCD2	2.2	BC012528	2.2	RFX5	2.2	SPRED1	2.1
PNKD	2.2	BHLHB9	2.2	NCAPD3	2.2	MPST	2.1
FANCG	2.2	WDR41	2.2	FBXL5	2.2	VSIG10	2.1
FAM117A	2.2	RAB8B	2.2	ATL3	2.2	LGALS8	2.1
PRPF38A	2.2	HSD17B7	2.2	THC2658991	2.2	PHOSPHO2-KLHL23	2.1

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ATF2	2.1	SHD	2.1	CDS2	2.1	DLAT	2.1
SETDB2	2.1	PLSCR1	2.1	FGFR1	2.1	CTDSPL	2.0
ZNF75D	2.1	LSM3	2.1	CREB3L2	2.1	ENST00000420759	2.0
ENST00000555011	2.1	LOC729887	2.1	THC2664860	2.1	CTAGE7P	2.0
GNE	2.1	PPP2R5E	2.1	KIF18B	2.1	IL4R	2.0
CB136271	2.1	MBOAT2	2.1	DAND5	2.1	C1orf106	2.0
DSCC1	2.1	THC2505678	2.1	XRCC1	2.1	SIX4	2.0
CKAP2L	2.1	ZNF492	2.1	GALM	2.1	UBR1	2.0
CCNB1	2.1	SRBD1	2.1	PLEKHF2	2.1	CLASP1	2.0
KIF3C	2.1	FAM100B	2.1	PEX14	2.1	S1PR5	2.0
RAB11FIP4	2.1	DENND1B	2.1	RAD54B	2.1	LRR1	2.0
RECK	2.1	HMGB3P1	2.1	FAM172A	2.1	PHTF1	2.0
C14orf23	2.1	FAM72D	2.1	CBX1	2.1	RIMKLB	2.0
FBXL20	2.1	SMC4	2.1	THC2637707	2.1	SCAMP1	2.0
STAT6	2.1	ERCC6L	2.1	HAUS3	2.1	IPP	2.0
LIN7B	2.1	WHSC1	2.1	DMRT3	2.1	DKK1	2.0
GALK2	2.1	ZBTB44	2.1	ANO6	2.1	XXYLT1	2.0
UBR7	2.1	CORT	2.1	CHM	2.1	ZFAND6	2.0
ATG4C	2.1	PXN	2.1	ZNF438	2.1	NUP43	2.0
RBL1	2.1	NFE2	2.1	OSBPL8	2.1	C7orf74	2.0
CDCA3	2.1	MTERFD3	2.1	CBX1	2.1	PLEKHA8	2.0
TTC32	2.1	BASP1	2.1	DUS4L	2.1	DERA	2.0
ECT2	2.1	WBP4	2.1	NPHP4	2.1	CASC5	2.0
HIST1H4H	2.1	TRAF7	2.1	LOC100132790	2.1	PTPN6	2.0
TOR1AIP2	2.1	FBXO36	2.1	SEC24A	2.1	BC067908	2.0
LINC00339	2.1	CCDC82	2.1	BX116014	2.1	PGM2L1	2.0
PARVA	2.1	HIST1H4I	2.1	PPP6C	2.1	ENST00000358073	2.0
PIGB	2.1	NPAT	2.1	BC029907	2.1	KLHL24	2.0
U2SURP	2.1	CA14	2.1	PCDH10	2.1	SMC3	2.0
ANKRD28	2.1	PAPSS2	2.1	OSBPL9	2.1	FANCI	2.0
TRIM53P	2.1	HIST1H4J	2.1	MITD1	2.1	PTER	2.0
COX11	2.1	TTC9C	2.1	WDR92	2.1	LOC100507265	2.0
RFC1	2.1	MEF2BNB	2.1	STEAP2	2.1	AK098220	2.0
THC2619545	2.1	PPM1F	2.1	LOC100505794	2.1	PRKD3	2.0
TMED8	2.1	VASH2	2.1	LOC400099	2.1	SLC25A13	2.0
INVS	2.1	PHF15	2.1	HILPDA	2.1	SCLT1	2.0
FAM114A1	2.1	IRAK1BP1	2.1	SCAI	2.1	LRP4	2.0
ZCCHC11	2.1	RILP	2.1	PGM2	2.1	KIFC1	2.0
LRRCC1	2.1	SPEG	2.1	ZBTB8A	2.1	GPD2	2.0
ENST00000450308	2.1	TTC7B	2.1	TMEM107	2.1	FANCM	2.0
ZDHHC20	2.1	LAYN	2.1	NUP43	2.1	GTF3C3	2.0

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ZNF277	2.0	PGM3	2.0	CD59	-2.0	MYO3B	-2.0
PTTG2	2.0	MUTED	2.0	THPO	-2.0	RAC2	-2.0
ZFP30	2.0	XPNPEP3	2.0	ZNF202	-2.0	HIST1H2BI	-2.0
FER	2.0	SNX10	2.0	TPRG1L	-2.0	THC2778685	-2.0
NDUFS1	2.0	THC2556546	2.0	AKT1	-2.0	NDFIP2	-2.0
ARHGAP12	2.0	DST	-2.0	SON	-2.0	ENST00000504184	-2.0
CCDC34	2.0	ZIC4	-2.0	POM121L12	-2.0	AFG3L2	-2.0
GSTM2P1	2.0	THC2507435	-2.0	SEMA5A	-2.0	KLC1	-2.0
DIAPH3	2.0	SMG5	-2.0	MBD3	-2.0	C9orf139	-2.0
RPL22L1	2.0	SUN5	-2.0	ATP2A2	-2.0	ZNF259	-2.0
DDX46	2.0	FAM55C	-2.0	POFUT2	-2.0	SLITRK6	-2.0
POT1	2.0	GAS5	-2.0	AP3D1	-2.0	DNASE1L2	-2.0
SLC24A1	2.0	PEF1	-2.0	POMZP3	-2.0	THC2559123	-2.0
SPRYD7	2.0	ANKS6	-2.0	SS18	-2.0	CD14	-2.0
SLC25A29	2.0	TEF	-2.0	GRPR	-2.0	FAM134C	-2.0
SKA2	2.0	POLR1C	-2.0	NXN	-2.0	GARS	-2.0
MSI2	2.0	ADRM1	-2.0	LRRC8B	-2.0	BRD4	-2.0
LOC100132815	2.0	C7	-2.0	BANP	-2.0	EHMT1	-2.0
MAT2B	2.0	LOC92249	-2.0	CFLAR	-2.0	CHRNE	-2.0
BAZ2B	2.0	CCDC57	-2.0	GNPTG	-2.0	BX105253	-2.0
LACE1	2.0	RNPS1	-2.0	ASRGL1	-2.0	CPNE7	-2.0
MAP3K13	2.0	GNAS	-2.0	TAF8	-2.0	COL4A5	-2.0
STRN	2.0	HDLBP	-2.0	TEX13B	-2.0	WFDC3	-2.0
CHAF1B	2.0	SNTG1	-2.0	LPPR2	-2.0	CYBA	-2.0
PTPRH	2.0	CASK	-2.0	MED10	-2.0	LOC100506528	-2.0
CERK	2.0	THC2660361	-2.0	ATF4	-2.0	NP101191	-2.0
TMEM194A	2.0	RBM22	-2.0	RAB36	-2.0	ZSCAN22	-2.0
SLC2A14	2.0	ZNF473	-2.0	USP10	-2.0	PRCC	-2.0
RPL39L	2.0	TMEM33	-2.0	BU903025	-2.0	ACAD8	-2.0
PPAPDC3	2.0	TIAM1	-2.0	LARP4B	-2.0	PDCD11	-2.0
BAD	2.0	DHX38	-2.0	TP53I11	-2.0	RAE1	-2.0
LOC100505806	2.0	MED18	-2.0	ACTG1	-2.0	AMN	-2.0
FADS1	2.0	CCNY	-2.0	UCN2	-2.0	C19orf6	-2.0
SNRPA1	2.0	ZMYND15	-2.0	SUV420H1	-2.0	SELPLG	-2.0
UBE2C	2.0	ENST00000427835	-2.0	ENST00000425471	-2.0	HM13	-2.0
ENST00000459691	2.0	NCOA5	-2.0	IMP4	-2.0	LOC96610	-2.0
HIST1H2AK	2.0	ANKRD40	-2.0	PRPH	-2.0	PLEKHF1	-2.0
TCFL5	2.0	REXO4	-2.0	UNC13D	-2.0	PES1	-2.0
CAPRIN2	2.0	CGB	-2.0	BC033528	-2.0	MED1	-2.0
ID2	2.0	ENST00000486256	-2.0	KIAA1875	-2.0	MIB2	-2.0
EMP2	2.0	PIK3IP1	-2.0	MMAB	-2.0	TP53TG3	-2.0

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SLC30A3	-2.0	THC2582296	-2.0	AI669333	-2.1	CRABP1	-2.1
P2RX6	-2.0	UBE2Z	-2.0	ENST00000448477	-2.1	CBFB	-2.1
ZIC5	-2.0	HNRNPA0	-2.0	BICD2	-2.1	OSCAR	-2.1
LRP10	-2.0	DNM1P46	-2.0	HES4	-2.1	DKK4	-2.1
SLC48A1	-2.0	LSG1	-2.0	LY86	-2.1	PMM2	-2.1
KLK9	-2.0	ZNF26	-2.0	POLR3E	-2.1	PRDM1	-2.1
DKFZp761E198	-2.0	DUSP23	-2.0	THC2673062	-2.1	RER1	-2.1
BC018099	-2.0	KIAA0090	-2.0	AF117899	-2.1	ELMO2	-2.1
SFTPA1	-2.0	LOC146880	-2.0	AJ005814	-2.1	CHST3	-2.1
ENST00000261651	-2.0	T	-2.0	CDH3	-2.1	CALY	-2.1
PSPH	-2.0	TMEM18	-2.0	SCAND2	-2.1	TTTY13	-2.1
BCL2L11	-2.0	C7orf26	-2.0	RRAD	-2.1	DIAPH2	-2.1
GLS	-2.0	GRP	-2.0	NEURL	-2.1	LPXN	-2.1
TCAP	-2.0	CCDC48	-2.0	UNC45A	-2.1	TCN2	-2.1
OPRK1	-2.0	SULT4A1	-2.0	LCE1C	-2.1	AL390214	-2.1
C16orf3	-2.0	MGA	-2.0	NDEL1	-2.1	ADRB3	-2.1
CAMK2D	-2.0	SDC3	-2.0	THC2538882	-2.1	AK024389	-2.1
LOC100131138	-2.0	NAPRT1	-2.0	WDR77	-2.1	C8orf31	-2.1
ACYP2	-2.0	MAGEA5	-2.0	GZMB	-2.1	IST1	-2.1
RLN3	-2.0	AF144054	-2.0	CEP85	-2.1	DUS1L	-2.1
ENST00000424133	-2.0	VWF	-2.0	AGPAT6	-2.1	TMEM97	-2.1
THC2660180	-2.0	PRRG3	-2.0	PNPLA2	-2.1	SLCO4A1	-2.1
CCDC93	-2.0	DIS3L2	-2.0	TMEM105	-2.1	RRP7A	-2.1
GCNT2	-2.0	TSSC4	-2.0	FOLR2	-2.1	FGFBP3	-2.1
ADCY4	-2.0	MAP4	-2.0	TMEM30A	-2.1	PITRM1	-2.1
FBXW8	-2.0	MTAP	-2.0	ACTN4	-2.1	MDM2	-2.1
NAPSA	-2.0	THC2707049	-2.0	TXNL4B	-2.1	TRIM21	-2.1
RUNDC1	-2.0	UBE2MP1	-2.0	FXYD5	-2.1	LRRC8D	-2.1
DFFA	-2.0	BCAS3	-2.0	TBC1D3P2	-2.1	HR	-2.1
CASP8	-2.0	NKTR	-2.0	DNAJB1	-2.1	M69012	-2.1
DKC1	-2.0	POM121L4P	-2.0	BMP7	-2.1	BC034319	-2.1
TOR1B	-2.0	ENST00000394813	-2.0	ZNF512B	-2.1	C1orf116	-2.1
BU625797	-2.0	DLL3	-2.0	ARMC7	-2.1	C5orf32	-2.1
TRIM26	-2.0	MYOZ3	-2.0	LOC494558	-2.1	THC2489404	-2.1
OMD	-2.0	RSPH1	-2.0	RNF135	-2.1	PYCR1	-2.1
FAM195A	-2.0	EXT2	-2.1	TMED9	-2.1	TMEM191B	-2.1
HIPK1	-2.0	FLNB	-2.1	ICOSLG	-2.1	LINC00328	-2.1
SERINC5	-2.0	THC2560938	-2.1	SPTBN1	-2.1	FLJ31713	-2.1
TRIM56	-2.0	OSR2	-2.1	POTEE	-2.1	PPP1R3D	-2.1
CD274	-2.0	SPDEF	-2.1	REXO1	-2.1	KLF13	-2.1
EVX1	-2.0	PCCB	-2.1	METTL21A	-2.1	THC2652817	-2.1

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SPATA2	-2.1	KRT81	-2.1	PEX5	-2.1	ATP11B	-2.1
SNCA	-2.1	HIST1H2AC	-2.1	RAB7B	-2.1	FLJ11235	-2.1
FTH1	-2.1	ZNF598	-2.1	THC2749298	-2.1	ENDOV	-2.1
ACTC1	-2.1	ERVH-3	-2.1	ZNF696	-2.1	CSH2	-2.1
MATN1	-2.1	LINC00265	-2.1	TMEM127	-2.1	FAM120A	-2.1
CYP2A13	-2.1	AK021432	-2.1	P4HB	-2.1	BG534208	-2.1
KLHL2	-2.1	B3GNT7	-2.1	OLFML2A	-2.1	ZP2	-2.1
GOLGA3	-2.1	MRPL49	-2.1	PRR22	-2.1	GLS2	-2.1
CACNB3	-2.1	CBS	-2.1	SEZ6L2	-2.1	BC015064	-2.1
ACE	-2.1	ING5	-2.1	SREBF2	-2.1	GON4L	-2.1
DNAH7	-2.1	TDRD1	-2.1	DEDD2	-2.1	TFEB	-2.1
AY358253	-2.1	GPR144	-2.1	BOD1	-2.1	ZNF167	-2.1
TMEM185B	-2.1	NAGPA	-2.1	C8orf73	-2.1	AF116688	-2.1
AF086468	-2.1	TRMT61A	-2.1	MTSS1L	-2.1	EMID1	-2.1
ATXN7L2	-2.1	TBC1D20	-2.1	LRRC34	-2.1	TNRC18	-2.1
WHSC2	-2.1	THC2765857	-2.1	BMP7	-2.1	WDR85	-2.1
PAQR7	-2.1	SAP18	-2.1	NPDC1	-2.1	ELMO3	-2.1
THC2572376	-2.1	ENST00000522026	-2.1	PPAPDC1A	-2.1	CDK5R2	-2.1
MSX2P1	-2.1	SUPT6H	-2.1	AGAP8	-2.1	LOC100653058	-2.1
PPY	-2.1	EPC1	-2.1	CPSF3L	-2.1	PEX5	-2.1
POTED	-2.1	ENST00000420724	-2.1	TRIM10	-2.1	PGAP3	-2.1
PALLD	-2.1	MBD1	-2.1	SLC2A9	-2.1	JRK	-2.1
DSTYK	-2.1	CAPN8	-2.1	ACSM2B	-2.1	THC2618461	-2.1
TRIM16L	-2.1	RRAS	-2.1	SUV420H1	-2.1	MAPK14	-2.1
SLC35E1	-2.1	CWC25	-2.1	EIF1	-2.1	PIK3R3	-2.1
AF161342	-2.1	ANKRD43	-2.1	POLR3A	-2.1	CRYGS	-2.1
PYGL	-2.1	GOLGA1	-2.1	SNHG12	-2.1	CXCL16	-2.1
FAM201A	-2.1	PAPLN	-2.1	BC063381	-2.1	BMS1	-2.1
B4GALNT4	-2.1	CTRL	-2.1	OR1F2P	-2.1	SIK1	-2.1
IFITM3	-2.1	CROT	-2.1	NPIPL2	-2.1	RGS3	-2.1
ZNF433	-2.1	DPT	-2.1	CNNM2	-2.1	SLC27A1	-2.1
BM695552	-2.1	MAX	-2.1	IL28A	-2.1	MOBP	-2.1
MGP	-2.1	RAF1	-2.1	UHMK1	-2.1	SERPINB9	-2.1
HSPB6	-2.1	MLL4	-2.1	BCAR1	-2.1	TMEM234	-2.1
SRP68	-2.1	SPIN3	-2.1	VCL	-2.1	RNF207	-2.1
NFYA	-2.1	RAB40B	-2.1	LRRC41	-2.1	SGSH	-2.1
PROSC	-2.1	TAF3	-2.1	GPRIN2	-2.1	LOC149703	-2.1
TAGLN2	-2.1	PIP4K2A	-2.1	MED10	-2.1	EWSR1	-2.1
KHDC1	-2.1	THC2568453	-2.1	C19orf28	-2.1	ALOX12B	-2.1
SLC23A2	-2.1	LSMD1	-2.1	OGT	-2.1	AZU1	-2.1
PRH2	-2.1	MAFK	-2.1	MAGED1	-2.1	PRR5	-2.1

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
PCSK7	-2.1	TTPAL	-2.1	SRSF8	-2.1	STRA6	-2.1
ARNTL2	-2.1	BATF3	-2.1	KCNH3	-2.1	BICD1	-2.1
LYPD2	-2.1	PTP4A1	-2.1	NAPRT1	-2.1	AK095453	-2.1
CHRNA7	-2.1	SOLH	-2.1	ENST00000514673	-2.1	ZSCAN12	-2.1
RPUSD4	-2.1	TCL6	-2.1	EIF1	-2.1	WIPI2	-2.1
CCND1	-2.1	SLC22A31	-2.1	THC2565608	-2.1	BCL11A	-2.1
THC2506535	-2.1	IQSEC1	-2.1	CCL3L3	-2.1	KANSL2	-2.1
THC2754061	-2.1	STAT3	-2.1	TRIM4	-2.1	TNFRSF12A	-2.1
ZNF500	-2.1	ENST00000445515	-2.1	JDP2	-2.1	EVC	-2.2
GPR182	-2.1	HEPACAM	-2.1	SEMA6A	-2.1	RNF166	-2.2
NADK	-2.1	CNNM1	-2.1	C21orf81	-2.1	DRD4	-2.2
POM121L1P	-2.1	TRMT61A	-2.1	ZNF440	-2.1	MRC2	-2.2
TOB1	-2.1	RAB11FIP1	-2.1	C22orf25	-2.1	RFNG	-2.2
AGPAT6	-2.1	COL27A1	-2.1	PRNP	-2.1	CEACAM1	-2.2
SERPINH1	-2.1	VAC14	-2.1	SEPP1	-2.1	NOC2L	-2.2
RAB11FIP1	-2.1	RBM8A	-2.1	ZNF853	-2.1	SSH3	-2.2
ASRGL1	-2.1	PCDHGA7	-2.1	IL32	-2.1	RPS2	-2.2
FOSL2	-2.1	DCX	-2.1	BC028022	-2.1	MED26	-2.2
ATF6B	-2.1	THC2565393	-2.1	C7orf40	-2.1	GPR119	-2.2
ITPR1	-2.1	ERN2	-2.1	MAMDC4	-2.1	SEC16A	-2.2
SPACA1	-2.1	GRB10	-2.1	VEGFA	-2.1	PRRC2B	-2.2
TMEM86B	-2.1	KCNMB4	-2.1	TMUB2	-2.1	PDK4	-2.2
CADM3	-2.1	NUMBL	-2.1	AK023077	-2.1	RRP7B	-2.2
ZNF346	-2.1	ITIH5	-2.1	DNAJA3	-2.1	FAM120C	-2.2
NSF	-2.1	KCNMA1	-2.1	PRMT5	-2.1	EP300	-2.2
THC2612889	-2.1	SLC13A2	-2.1	CLASRP	-2.1	CLK4	-2.2
ZC3HAV1	-2.1	HEATR7A	-2.1	THC2510958	-2.1	CLK2	-2.2
FOSB	-2.1	TMEM43	-2.1	AATK	-2.1	ODC1	-2.2
S72604	-2.1	PIEZO1	-2.1	PHLDA2	-2.1	ZNF418	-2.2
B3GNT9	-2.1	HBEGF	-2.1	CPT1A	-2.1	FLJ45340	-2.2
AF113013	-2.1	KIAA0319L	-2.1	C10orf35	-2.1	TM7SF3	-2.2
FAM178B	-2.1	LOC100506972	-2.1	YIPF2	-2.1	FXR2	-2.2
C6orf48	-2.1	RCN1	-2.1	AF126109	-2.1	C10orf27	-2.2
PKNOX1	-2.1	SIX2	-2.1	SLC9A1	-2.1	AK000313	-2.2
LOC100505711	-2.1	SRM	-2.1	SRP68	-2.1	PURA	-2.2
KLRG2	-2.1	TNRC18	-2.1	THC2519072	-2.1	SCGB1A1	-2.2
CDK5RAP3	-2.1	NCLN	-2.1	BRF1	-2.1	COL4A1	-2.2
AK023954	-2.1	LDLRAP1	-2.1	FOXS1	-2.1	SLITRK1	-2.2
C1orf187	-2.1	NAT9	-2.1	SLC25A47	-2.1	OR7A10	-2.2
RPL28	-2.1	AK097259	-2.1	ZDHHC23	-2.1	Z25424	-2.2
CHPF2	-2.1	SLC31A1	-2.1	GGT7	-2.1	C7orf53	-2.2

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
JUNB	-2.2	TPD52L2	-2.2	GOLGA8A	-2.2	PLA2G2D	-2.2
TXNDC11	-2.2	UCP2	-2.2	FAT1	-2.2	DAB2	-2.2
CCDC166	-2.2	INHBC	-2.2	EIF5	-2.2	ACAD10	-2.2
XPC	-2.2	TMEM191A	-2.2	NYX	-2.2	INE1	-2.2
C9orf50	-2.2	VAMP1	-2.2	ZNF434	-2.2	KCNK15	-2.2
ELK4	-2.2	SLC9A8	-2.2	GGT3P	-2.2	CTRL	-2.2
RBM23	-2.2	THC2668327	-2.2	MAP6D1	-2.2	ARSA	-2.2
PRSS2	-2.2	LRPAP1	-2.2	DLL3	-2.2	LAT	-2.2
UFM1	-2.2	BF985168	-2.2	RGR	-2.2	BX097486	-2.2
GLIS3	-2.2	GMPPB	-2.2	TM6SF2	-2.2	PILRB	-2.2
CAMK2D	-2.2	SOBP	-2.2	USP22	-2.2	MFI2	-2.2
UNC13B	-2.2	SUGP2	-2.2	SNORA70	-2.2	CLK2	-2.2
ZNF84	-2.2	AATF	-2.2	STK35	-2.2	KDELR2	-2.2
NLRC3	-2.2	ULK3	-2.2	LUC7L	-2.2	ADSSL1	-2.2
AK074670	-2.2	CA314185	-2.2	IGFBPL1	-2.2	YIF1B	-2.2
AFG3L1P	-2.2	PRSS8	-2.2	POTEG	-2.2	ENST00000523617	-2.2
POTEG	-2.2	FAM59A	-2.2	ITSN2	-2.2	GGT7	-2.2
KIFC2	-2.2	TTC21A	-2.2	MYLIP	-2.2	SDK1	-2.2
MRFAP1	-2.2	AFF4	-2.2	MTRF1L	-2.2	LOC100128682	-2.2
PLAGL1	-2.2	MON1A	-2.2	TTI2	-2.2	THNSL1	-2.2
PRM3	-2.2	C2	-2.2	SHISA4	-2.2	CYP1A2	-2.2
ENST00000424245	-2.2	AF264627	-2.2	VCP	-2.2	LENG8	-2.2
CRCP	-2.2	BAIAP2	-2.2	SDSL	-2.2	PCBD2	-2.2
RGNEF	-2.2	THADA	-2.2	FBXO25	-2.2	POU5F1P3	-2.2
THC2644897	-2.2	ZNF783	-2.2	ZNF134	-2.2	PITHD1	-2.2
MAPT	-2.2	FGD2	-2.2	FLJ10661	-2.2	RRN3	-2.2
EGFL8	-2.2	CR604497	-2.2	SEC13	-2.2	TSPAN8	-2.2
TPCN1	-2.2	ARNTL2	-2.2	SPDYE1	-2.2	ZNF2	-2.2
THC2751913	-2.2	AK026140	-2.2	NOP14	-2.2	SLC25A46	-2.2
DOK3	-2.2	NEBL	-2.2	AK021744	-2.2	TAP1	-2.2
MLXIP	-2.2	CYP4F30P	-2.2	ARHGEF10	-2.2	LMTK2	-2.2
CACNG8	-2.2	CDK20	-2.2	AB007971	-2.2	AF074982	-2.2
BX102988	-2.2	ENST00000390265	-2.2	SNX12	-2.2	SEMA6A	-2.2
PITX1	-2.2	SLC16A9	-2.2	RSPH4A	-2.2	SRRT	-2.2
POLH	-2.2	HIST1H2BM	-2.2	THC2657512	-2.2	GOLGA6A	-2.2
UFM1	-2.2	OPTN	-2.2	MFI2	-2.2	ENST00000446344	-2.2
CR616772	-2.2	NOB1	-2.2	CTBS	-2.2	BC003519	-2.2
OPN4	-2.2	TPM4	-2.2	KHSRP	-2.2	HERC6	-2.2
ADAMTS2	-2.2	COL5A2	-2.2	DCDC5	-2.2	ACRBP	-2.2
S100A16	-2.2	EIF4G1	-2.2	CCNL2	-2.2	C1orf177	-2.2
SPATA4	-2.2	BMS1	-2.2	H6PD	-2.2	SLC22A17	-2.2

Appendix VI Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
GMEB2	-2.2	C17orf88	-2.2	DNHD1	-2.2	MLLT1	-2.3
ATXN1L	-2.2	PANX2	-2.2	TMEM30A	-2.2	RIIAD1	-2.3
FCGR2A	-2.2	ASNS	-2.2	MAN2A2	-2.2	C19orf24	-2.3
CELF4	-2.2	RNF145	-2.2	TNXB	-2.2	ZNF236	-2.3
GPSM3	-2.2	NEUROG1	-2.2	GGT1	-2.2	PRKAB2	-2.3
MDN1	-2.2	TMEM8A	-2.2	PHF14	-2.2	USP22	-2.3
PES1	-2.2	TEX261	-2.2	BX647159	-2.2	UNKL	-2.3
CLDN19	-2.2	AF009267	-2.2	ISL2	-2.2	EDEM3	-2.3
THC2727494	-2.2	MINA	-2.2	PHC2	-2.2	NEU4	-2.3
STOML1	-2.2	CECR7	-2.2	POU3F1	-2.2	BLVRB	-2.3
ANKMY1	-2.2	ZDHHC21	-2.2	CU674743	-2.2	ENST00000431001	-2.3
ENST00000467537	-2.2	PDRG1	-2.2	NUBP1	-2.2	RRP9	-2.3
DNAJB4	-2.2	IRX4	-2.2	CREBBP	-2.2	POM121	-2.3
GTPBP5	-2.2	RHOV	-2.2	CSRNP1	-2.2	GPR115	-2.3
CHAD	-2.2	MEGF6	-2.2	RRAS	-2.2	FUCA1	-2.3
NFX1	-2.2	SARS	-2.2	KIAA0090	-2.2	CHADL	-2.3
TOMM40	-2.2	ENST00000445770	-2.2	COL3A1	-2.2	DIS3L2	-2.3
TM6SF1	-2.2	DPYSL4	-2.2	MBD1	-2.2	LOC100130071	-2.3
ZNF467	-2.2	EMX1	-2.2	C19orf43	-2.2	ITGB1	-2.3
GALR2	-2.2	LOC100507654	-2.2	TMEM239	-2.2	MSTO1	-2.3
NIPAL2	-2.2	SULT1A1	-2.2	AF086536	-2.2	AKR1A1	-2.3
RHOV	-2.2	SPEN	-2.2	FLJ45340	-2.2	CASP14	-2.3
PILRA	-2.2	SUSD2	-2.2	THC2657554	-2.2	ZFHX2	-2.3
FAM8A1	-2.2	C16orf11	-2.2	C1orf226	-2.2	U2AF2	-2.3
GUSBP1	-2.2	ZNF551	-2.2	ZNFX1	-2.2	LAMC2	-2.3
NACA	-2.2	FBXO17	-2.2	GPATCH4	-2.2	MICAL3	-2.3
KGFLP2	-2.2	ENST00000391654	-2.2	CDON	-2.2	HEATR6	-2.3
URB1	-2.2	AK090463	-2.2	TMEM41A	-2.2	BM678681	-2.3
THC2558776	-2.2	RAD23A	-2.2	IQSEC2	-2.2	LINC00476	-2.3
EMID1	-2.2	HNRNPAB	-2.2	CCND1	-2.2	TPM4	-2.3
CSF3R	-2.2	LOC729603	-2.2	NXNL1	-2.2	LOC286161	-2.3
C10orf2	-2.2	RPS6KA2	-2.2	CD274	-2.2	CD59	-2.3
AK074162	-2.2	GRID2	-2.2	PSEN2	-2.2	FOXN1	-2.3
SEZ6L2	-2.2	DLC1	-2.2	RRP12	-2.3	RETSAT	-2.3
SMARCA4	-2.2	TOMM40	-2.2	THC2686813	-2.3	NPFFR1	-2.3
ECE1	-2.2	RABGAP1L	-2.2	LRP1	-2.3	MKNK2	-2.3
ITPK1	-2.2	MTRNR2L6	-2.2	SNCA	-2.3	SPRY2	-2.3
CNTN1	-2.2	SNHG8	-2.2	POM121	-2.3	PRSS23	-2.3
AK097166	-2.2	PCSK7	-2.2	THC2612025	-2.3	STEAP3	-2.3
ENST00000480694	-2.2	CACNA1A	-2.2	RNPS1	-2.3	POLR3H	-2.3
BAX	-2.2	CACNA1S	-2.2	PKD1	-2.3	FLJ45340	-2.3

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
BF926494	-2.3	ITGB1	-2.3	UPK3B	-2.3	BC021053	-2.3
ATP1B1	-2.3	MAFG	-2.3	AI198876	-2.3	KCTD15	-2.3
PSORS1C2	-2.3	SRRM2	-2.3	C22orf15	-2.3	AK097166	-2.3
ZSCAN18	-2.3	RALGDS	-2.3	CD276	-2.3	CR745430	-2.3
PCSK1N	-2.3	PCP4L1	-2.3	MKRN1	-2.3	GNL3L	-2.3
SCUBE1	-2.3	MGA	-2.3	ZNF692	-2.3	DDX17	-2.3
PAFAH2	-2.3	AK090442	-2.3	ENST00000449023	-2.3	PARD6A	-2.3
CST3	-2.3	SCARNA17	-2.3	SLC26A1	-2.3	ENST00000423008	-2.3
OSMR	-2.3	ENPP7	-2.3	OTUD7A	-2.3	RNF217	-2.3
BF509345	-2.3	PTPRJ	-2.3	SPDYE3	-2.3	TRIM44	-2.3
KDM2A	-2.3	SYNGR2	-2.3	PPM1E	-2.3	GRB10	-2.3
FAM179A	-2.3	EWSR1	-2.3	RBM14	-2.3	RASL11A	-2.3
LOC154822	-2.3	SAMD4B	-2.3	SLC46A1	-2.3	ANKRD20A2	-2.3
RPL27A	-2.3	KCTD13	-2.3	ABCF2	-2.3	HIRA	-2.3
EMD	-2.3	SCFD2	-2.3	KEAP1	-2.3	LGALS7B	-2.3
ROBO3	-2.3	ENST00000512848	-2.3	ALPPL2	-2.3	SLC46A1	-2.3
GPBAR1	-2.3	GTPBP5	-2.3	TDRD7	-2.3	BRD2	-2.3
POU5F1	-2.3	APBA2	-2.3	BRWD1-IT2	-2.3	THC2743652	-2.3
KGFLP1	-2.3	LOC100506075	-2.3	KCNJ14	-2.3	THC2539923	-2.3
PPP1R15A	-2.3	GPT2	-2.3	BANP	-2.3	MAN2A2	-2.3
THC2731608	-2.3	TSPAN14	-2.3	CD82	-2.3	INHBE	-2.3
ATXN2L	-2.3	MYOM2	-2.3	NUP210	-2.3	ENST00000390543	-2.3
C7orf50	-2.3	THC2563307	-2.3	THC2660636	-2.3	ADRA2A	-2.3
SYT5	-2.3	CLK3	-2.3	CUL9	-2.3	LOC388588	-2.3
LOC388796	-2.3	KCNA7	-2.3	OXT	-2.3	KLHL35	-2.3
AKNA	-2.3	UBXN8	-2.3	CU687617	-2.3	TMEM30B	-2.3
TIGD3	-2.3	TMEM9B	-2.3	STIP1	-2.3	MTRF1L	-2.3
OR1N2	-2.3	AF090890	-2.3	ZNF397	-2.3	SF3A2	-2.3
SPRR2E	-2.3	RBM8A	-2.3	ENST00000447206	-2.3	THC2772705	-2.3
ITGA2	-2.3	TIMM44	-2.3	BBC3	-2.3	ZFR2	-2.3
DRAM1	-2.3	TRIM68	-2.3	TRPV6	-2.3	ITSN2	-2.3
ENST00000553155	-2.3	NRIP2	-2.3	NCOA7	-2.3	SF1	-2.3
THC2559929	-2.3	OR1F2P	-2.3	ZXDC	-2.3	TPM4	-2.3
FAM129C	-2.3	CARNS1	-2.3	HKR1	-2.3	ABCA3	-2.3
TPRN	-2.3	SARM1	-2.3	THC2724451	-2.3	EPN3	-2.3
CCDC57	-2.3	KCTD15	-2.3	KIAA1161	-2.3	SIRPA	-2.3
C15orf59	-2.3	PI4KAP2	-2.3	LOC100131170	-2.3	USF2	-2.3
SHISA7	-2.3	FKRP	-2.3	ZCCHC12	-2.3	ABHD4	-2.3
LOC253039	-2.3	KMO	-2.3	TTC17	-2.3	WDR20	-2.3
ACYP2	-2.3	HERC5	-2.3	PMEL	-2.3	MAN2C1	-2.3
CD7	-2.3	ACAP1	-2.3	CAMKK1	-2.3	GOSR2	-2.3

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
C9orf167	-2.3	ENST00000331856	-2.4	ANKRD24	-2.4	LMOD2	-2.4
IRF1	-2.3	CTBP1	-2.4	ANKRD22	-2.4	METTL19	-2.4
HABP4	-2.3	NP511100	-2.4	SRCAP	-2.4	FAM113A	-2.4
LOC100505746	-2.3	ARHGEF15	-2.4	SPDYE3	-2.4	FAM71E1	-2.4
TMSB10	-2.3	ZFYVE28	-2.4	CATSPER3	-2.4	LSG1	-2.4
TJAP1	-2.3	ADAMTS13	-2.4	SHC2	-2.4	R3HDM2	-2.4
BX113029	-2.3	C22orf15	-2.4	ENDOD1	-2.4	JAK3	-2.4
PQLC2	-2.3	THC2656826	-2.4	SH3RF2	-2.4	TTC17	-2.4
MED29	-2.3	TMEM114	-2.4	LARP1	-2.4	BG462058	-2.4
ELF5	-2.3	DENND2A	-2.4	RBM14	-2.4	DDX56	-2.4
EI24	-2.3	TMEM38A	-2.4	SRRT	-2.4	FBP1	-2.4
CNTNAP3B	-2.3	CPAMD8	-2.4	ITPKC	-2.4	AK022609	-2.4
AK001094	-2.3	ZMAT1	-2.4	INTS5	-2.4	CR606969	-2.4
AK000832	-2.3	POLR3H	-2.4	OLFM2	-2.4	LRRC46	-2.4
ENST00000431987	-2.3	THC2739159	-2.4	GRK1	-2.4	GLTPD1	-2.4
SUMF2	-2.3	CEP97	-2.4	C3orf62	-2.4	PI4K2A	-2.4
CCDC64B	-2.3	MYLIP	-2.4	TMED3	-2.4	ASRGL1	-2.4
C9orf43	-2.3	NAB1	-2.4	FOXK2	-2.4	SIRT7	-2.4
IMPAD1	-2.3	H15635	-2.4	ALDH3B1	-2.4	SIRPB1	-2.4
SGCA	-2.3	COL20A1	-2.4	THC2742806	-2.4	FAM82A2	-2.4
HYAL1	-2.3	BCAN	-2.4	CEBPE	-2.4	KGFLP1	-2.4
LTB	-2.3	TCP10L2	-2.4	CYP2D6	-2.4	BF510844	-2.4
C16orf86	-2.3	KRTAP13-4	-2.4	DNAJB2	-2.4	MKRN9P	-2.4
ITFG2	-2.4	TXLNA	-2.4	GOT1	-2.4	ENST00000553378	-2.4
ACAP3	-2.4	ASRGL1	-2.4	CECR5-AS1	-2.4	HIPK2	-2.4
FKSG83	-2.4	ANKRD11	-2.4	FAM70B	-2.4	CNOT4	-2.4
HHLA3	-2.4	EBI3	-2.4	ENST00000450467	-2.4	GGT1	-2.4
MRO	-2.4	ZIC1	-2.4	ADAMTS16	-2.4	BC042649	-2.4
AB075822	-2.4	ANKFY1	-2.4	AK056855	-2.4	LRRC37A3	-2.4
MTCH1	-2.4	C21orf88	-2.4	TUBE1	-2.4	CAPN12	-2.4
DUSP2	-2.4	GLS	-2.4	EIF4H	-2.4	AK090397	-2.4
MPPED2	-2.4	RGMB	-2.4	CCDC88C	-2.4	RNF157	-2.4
KIAA0889	-2.4	NCF1	-2.4	IGLL1	-2.4	PELO	-2.4
RUNDC3A	-2.4	ZSCAN1	-2.4	AK127132	-2.4	AP3S2	-2.4
TMC8	-2.4	MEFV	-2.4	IBA57	-2.4	CCDC142	-2.4
THC2557626	-2.4	CTF1	-2.4	ZNF544	-2.4	ENST00000495094	-2.4
HIVEP3	-2.4	TXNDC11	-2.4	NAT8L	-2.4	ATOH7	-2.4
THC2553569	-2.4	C1orf54	-2.4	ASB8	-2.4	C9orf174	-2.4
THC2761218	-2.4	IL17D	-2.4	SETD5	-2.4	GNA11	-2.4
ENST00000422957	-2.4	AK022183	-2.4	AFG3L2	-2.4	CHRNA4	-2.4
KCNN2	-2.4	CLN8	-2.4	TMEM26	-2.4	THC2710559	-2.4

Appendix VI Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
GRM5	-2.4	HYOU1	-2.4	GTPBP4	-2.5	THC2677037	-2.5
CREG1	-2.4	DNASE2	-2.4	THC2548869	-2.5	AK125099	-2.5
LRRN2	-2.4	TH1L	-2.4	THC2534528	-2.5	AK000707	-2.5
USP4	-2.4	VWDE	-2.4	MUC17	-2.5	FLJ32955	-2.5
KRT3	-2.4	BC127746	-2.4	INSL3	-2.5	OR11A1	-2.5
MED29	-2.4	AK025430	-2.4	MAMSTR	-2.5	GRINA	-2.5
DHCR24	-2.4	CLEC3B	-2.4	CRK	-2.5	PPME1	-2.5
THC2506382	-2.4	TNFAIP3	-2.4	MYL7	-2.5	RGS22	-2.5
NUPR1	-2.4	PLAGL1	-2.4	BM807051	-2.5	RIBC2	-2.5
THC2548567	-2.4	CD164	-2.4	THC2687398	-2.5	GPT2	-2.5
FICD	-2.4	FEM1A	-2.4	KIR2DL4	-2.5	EPDR1	-2.5
KIAA0664	-2.4	PUS1	-2.4	USP18	-2.5	ZXDC	-2.5
ENST00000398878	-2.4	TSPYL2	-2.4	PITPNA	-2.5	GORASP1	-2.5
AF242527	-2.4	GLIS2	-2.4	ANKRD20A5P	-2.5	ZNF768	-2.5
PLEKHG1	-2.4	HOPX	-2.4	CTSK	-2.5	THC2539541	-2.5
MAN2B2	-2.4	PSPH	-2.4	MUL1	-2.5	MFHAS1	-2.5
DGCR8	-2.4	ENST00000390601	-2.4	SPG20OS	-2.5	AK094623	-2.5
BC031250	-2.4	HRASLS5	-2.4	SOCS1	-2.5	CTSH	-2.5
GPX3	-2.4	ATF6B	-2.4	PRKCDBP	-2.5	CU690321	-2.5
OR10H3	-2.4	ADHFE1	-2.4	AK096031	-2.5	LOC399900	-2.5
SMG7	-2.4	MTA1	-2.4	TM9SF4	-2.5	ENST00000471090	-2.5
SMG9	-2.4	ENST00000435714	-2.4	HIPK2	-2.5	RBM4	-2.5
POFUT2	-2.4	FLJ23867	-2.4	LTBP4	-2.5	LOC100506990	-2.5
ZNF335	-2.4	ODF4	-2.4	TEP1	-2.5	CEND1	-2.5
OR3A3	-2.4	C6orf81	-2.4	CYTH2	-2.5	ANGPTL6	-2.5
BM683477	-2.4	LOC729915	-2.4	S100P	-2.5	F5	-2.5
IL17A	-2.4	ENST00000404223	-2.4	CHMP7	-2.5	PDE3A	-2.5
ENST00000532821	-2.4	AK000420	-2.4	ADAMTSL5	-2.5	LONRF1	-2.5
SASH1	-2.4	KLF2	-2.4	CSPG5	-2.5	CES2	-2.5
AJ295982	-2.4	AMIGO1	-2.4	GNRHR2	-2.5	ORMDL3	-2.5
C14orf102	-2.4	TRIB3	-2.4	ZNF568	-2.5	ENST00000390294	-2.5
SLC22A11	-2.4	CSH1	-2.4	ADCK2	-2.5	GOT1	-2.5
MYO1E	-2.4	JRK	-2.4	MAPT	-2.5	XPNPEP2	-2.5
PDE12	-2.4	ENST00000436263	-2.5	TNFRSF1A	-2.5	H6PD	-2.5
ARHGAP30	-2.4	AK056449	-2.5	VAMP2	-2.5	AK022183	-2.5
AGAP7	-2.4	PDGFB	-2.5	BE672039	-2.5	DQX1	-2.5
SGSM1	-2.4	RASGEF1C	-2.5	SLC1A5	-2.5	THC2517566	-2.5
ENST00000419836	-2.4	THC2697642	-2.5	AA188598	-2.5	C19orf23	-2.5
ZNF174	-2.4	POP1	-2.5	GNA11	-2.5	ACTA1	-2.5
KCNK10	-2.4	CSHL1	-2.5	PKD1	-2.5	ADAMTSL4	-2.5
C12orf34	-2.4	CTRB2	-2.5	PDE12	-2.5	PP7080	-2.5

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
LCK	-2.5	DNAI2	-2.5	ANKRD20A2	-2.6	EHD3	-2.6
C6orf145	-2.5	XPO6	-2.5	PANX2	-2.6	NPIP	-2.6
KLHL21	-2.5	NADK	-2.5	NDRG1	-2.6	SPATA18	-2.6
DYSF	-2.5	BU929651	-2.5	GNA12	-2.6	MIRLET7BHG	-2.6
ILF3	-2.5	METTL21A	-2.5	DTX2	-2.6	FOXO3	-2.6
COL18A1	-2.5	LRRC36	-2.5	ABI3	-2.6	TMEM79	-2.6
BF972140	-2.5	FKSG43	-2.5	ANKRD53	-2.6	MEOX2	-2.6
PANX3	-2.5	BTBD9	-2.5	FBXO27	-2.6	ZNF615	-2.6
DNAJB2	-2.5	XCR1	-2.5	KCNQ1OT1	-2.6	DDX60L	-2.6
ASMTL-AS1	-2.5	CLEC18B	-2.5	MGAT5	-2.6	AF116720	-2.6
PRAME	-2.5	THC2659814	-2.5	ANTXR1	-2.6	THC2657657	-2.6
THC2655552	-2.5	FBRSL1	-2.5	E4F1	-2.6	THC2712372	-2.6
ENST00000474213	-2.5	RUNDC3B	-2.5	NP111770	-2.6	NP274062	-2.6
MYH6	-2.5	GGT1	-2.5	GGTLC1	-2.6	GBA2	-2.6
THC2646741	-2.5	RAMP1	-2.5	PLEC	-2.6	FAM174B	-2.6
TRIM41	-2.5	DQ786249	-2.5	TOR3A	-2.6	STEAP3	-2.6
LOC100653218	-2.5	LPP	-2.5	CCDC78	-2.6	RNPEP	-2.6
SHISA9	-2.5	IFITM1	-2.5	TNPO2	-2.6	USE1	-2.6
STAT3	-2.5	AK026869	-2.5	GOLGA8IP	-2.6	BAG3	-2.6
SLC5A3	-2.5	COMMD7	-2.5	TMEM9B	-2.6	ATP1A4	-2.6
LOC441204	-2.5	GATM	-2.5	CDC42SE1	-2.6	CHMP7	-2.6
CYP2F1	-2.5	LOC642838	-2.5	HEATR8	-2.6	GGT2	-2.6
TYROBP	-2.5	PGS1	-2.5	S100A3	-2.6	P2RX3	-2.6
VMAC	-2.5	HLA-C	-2.5	FAM123A	-2.6	MFSD6L	-2.6
FTCD	-2.5	PDPK1	-2.5	SLC35E1	-2.6	FADS6	-2.6
WDR73	-2.5	JMJD5	-2.5	HAND1	-2.6	ACBD7	-2.6
THEM5	-2.5	COX19	-2.5	LAMB2	-2.6	C3orf51	-2.6
FAM120AOS	-2.5	THC2506246	-2.5	ATN1	-2.6	MYLPF	-2.6
TNFRSF10B	-2.5	S100A1	-2.5	RFPL3-AS1	-2.6	THC2730423	-2.6
HDAC4	-2.5	THC2717023	-2.5	HK3	-2.6	AHNAK2	-2.6
LOC100507588	-2.5	CRK	-2.5	ZNF346	-2.6	ANKRD20A2	-2.6
ACTR5	-2.5	SLC25A37	-2.5	SSH1	-2.6	IL15RA	-2.6
ZBTB7B	-2.5	CD6	-2.5	SRPRB	-2.6	THC2698405	-2.6
ENST00000326333	-2.5	DPH2	-2.5	FAIM2	-2.6	X03757	-2.6
POLR3E	-2.5	C1orf88	-2.5	TMC4	-2.6	KLF13	-2.6
CU690935	-2.5	PRR3	-2.5	MYADM	-2.6	SLCO2A1	-2.6
MYL2	-2.5	XAF1	-2.5	SMR3A	-2.6	LOC100653245	-2.6
MMP15	-2.5	NOP56	-2.5	TRIM74	-2.6	C8G	-2.6
MAPK8IP3	-2.5	USP7	-2.5	TXNDC2	-2.6	LILRA1	-2.6
ENST00000440703	-2.5	RIMBP2	-2.5	POM121L1P	-2.6	PHKA1	-2.6
MAPK15	-2.5	THC2621221	-2.5	GALNT2	-2.6	IDS	-2.6

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
HTR3A	-2.6	C2orf72	-2.6	ARID1A	-2.7	CGB1	-2.7
ACTG1	-2.6	EIF5A2	-2.6	HMX2	-2.7	EEF2	-2.7
GPR61	-2.6	ACTB	-2.6	ADA	-2.7	MLXIP	-2.7
C20orf3	-2.6	DDIT3	-2.6	POLR2A	-2.7	POLM	-2.7
SYNPO2	-2.6	THC2766373	-2.6	FLT4	-2.7	THC2694242	-2.7
BX647685	-2.6	ENST00000414544	-2.6	KDM4A	-2.7	SLC7A11	-2.7
PLS3	-2.6	C6orf10	-2.6	ULK3	-2.7	RAPGEF1	-2.7
IZUMO4	-2.6	TRIO	-2.6	FBLN7	-2.7	UBE2L6	-2.7
THC2718728	-2.6	CDC42EP1	-2.6	C1orf183	-2.7	THC2781239	-2.7
COQ9	-2.6	FW340012	-2.6	REN	-2.7	THC2584954	-2.7
EAF1	-2.6	TFRC	-2.6	AF010144	-2.7	LOC100505549	-2.7
BC011805	-2.6	LY6D	-2.6	ENST00000491977	-2.7	TNXB	-2.7
TXNRD1	-2.6	GOT2	-2.6	TXNIP	-2.7	ALDOC	-2.7
PHF23	-2.6	STAT3	-2.6	KIAA1652	-2.7	ENST00000548210	-2.7
PCBD2	-2.6	ZNF276	-2.6	WNK2	-2.7	GIMAP8	-2.7
GRINA	-2.6	THC2758056	-2.6	ENST00000397094	-2.7	ARHGAP22	-2.7
DA093175	-2.6	PCSK6	-2.6	KIAA0513	-2.7	RASSF1	-2.7
MYC	-2.6	HLA-E	-2.6	STAP2	-2.7	THC2621771	-2.7
SGK223	-2.6	DAP	-2.6	ZFPM2	-2.7	GGTLC2	-2.7
AGAP7	-2.6	CCDC149	-2.6	GHSR	-2.7	C17orf108	-2.7
KCNA7	-2.6	DKK3	-2.6	ZNF506	-2.7	FOXO3	-2.7
ACAD10	-2.6	AK124882	-2.6	SLC6A20	-2.7	TEX101	-2.7
C1QTNF4	-2.6	ENST00000469997	-2.6	MVP	-2.7	ZNFX1	-2.7
ENST00000360902	-2.6	FIBCD1	-2.6	TNPO2	-2.7	PARK2	-2.7
ZNF585B	-2.6	HAMP	-2.6	C12orf68	-2.7	PPP1R3F	-2.7
DNAJB4	-2.6	NOP2	-2.7	MUC4	-2.7	ZFAND3	-2.7
NPIPL3	-2.6	SURF6	-2.7	CLK2	-2.7	IMP5	-2.7
NOMO1	-2.6	NCDN	-2.7	TRPV1	-2.7	KLK5	-2.7
S72422	-2.6	AL110237	-2.7	RASL12	-2.7	ITGB1BP2	-2.7
AW874684	-2.6	THC2546394	-2.7	TRIM27	-2.7	ZNF689	-2.7
WDR1	-2.6	ARHGAP27	-2.7	GPR21	-2.7	ACOX2	-2.7
ITGA7	-2.6	MXRA8	-2.7	LOC100132247	-2.7	ITM2C	-2.7
SOX7	-2.6	AA837799	-2.7	PELI2	-2.7	MMP28	-2.7
ABCA2	-2.6	GJD4	-2.7	NCKIPSD	-2.7	DNAJC11	-2.7
ZDHHC21	-2.6	MATN1	-2.7	FTSJ2	-2.7	RNASET2	-2.7
FAM95B1	-2.6	MLYCD	-2.7	ITFG2	-2.7	PDLIM5	-2.7
PAQR6	-2.6	FBXO2	-2.7	MIDN	-2.7	TRIM25	-2.7
NCOA7	-2.6	MYBBP1A	-2.7	THC2702650	-2.7	CFLAR	-2.7
UBQLN4	-2.6	MON1B	-2.7	AK023447	-2.7	GGTLC2	-2.7
CARD9	-2.6	LTB4R	-2.7	OSBPL10	-2.7	ZRSR2	-2.7
BC030138	-2.6	ANKRD20A2	-2.7	MLLT1	-2.7	ZNF407	-2.7

Appendix VI Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
RAP1GAP2	-2.7	LOC100130456	-2.7	RNASE1	-2.8	LARP1	-2.8
TRAK1	-2.7	LAMA5	-2.7	LOC90499	-2.8	RABGAP1L	-2.8
SNAI1	-2.7	PDLIM5	-2.7	PSAP	-2.8	SULT4A1	-2.8
PABPC4	-2.7	RUNDC2C	-2.7	POM121L4P	-2.8	POM121L8P	-2.8
THC2663783	-2.7	BC036431	-2.7	VPS13D	-2.8	THC2600736	-2.8
CHPF2	-2.7	NKX1-2	-2.7	HRC	-2.8	RSL1D1	-2.8
HIST2H2AA4	-2.7	UBE2J2	-2.7	LCE4A	-2.8	THC2754464	-2.8
DDX31	-2.7	TRIM41	-2.7	TPM1	-2.8	TMEM89	-2.8
MMP23B	-2.7	ISG20	-2.8	C9orf9	-2.8	EWSR1	-2.8
SIGLEC6	-2.7	BCL2L11	-2.8	ACTG1	-2.8	TRIM36	-2.8
AW576858	-2.7	MYBPC2	-2.8	MASP2	-2.8	TMIE	-2.8
ITGB2	-2.7	LRIT1	-2.8	HAPLN3	-2.8	NFIB	-2.8
THC2735727	-2.7	CCDC86	-2.8	HIPK2	-2.8	TNS3	-2.8
C20orf165	-2.7	PHKG1	-2.8	GNA12	-2.8	MYH9	-2.8
ZBTB40	-2.7	THC2674191	-2.8	ALAS1	-2.8	PCSK6	-2.8
LRIG1	-2.7	FOXP3	-2.8	ZBTB46	-2.8	NISCH	-2.8
SLC22A14	-2.7	STMN1	-2.8	IL1RL2	-2.8	ENST00000312015	-2.8
PANK2	-2.7	ENST00000356023	-2.8	LAT	-2.8	MAL	-2.8
LOC100132247	-2.7	LIMS2	-2.8	MDM2	-2.8	THC2679226	-2.8
MARS	-2.7	PCLO	-2.8	TMEM171	-2.8	CYP11A1	-2.8
ENST00000441316	-2.7	FSD2	-2.8	KCNN4	-2.8	THC2726959	-2.8
NBEA	-2.7	LOC284933	-2.8	THC2729109	-2.8	TP73-AS1	-2.8
TNFSF9	-2.7	PDXDC2P	-2.8	RPL13	-2.8	APBA2	-2.8
ENST00000553312	-2.7	EPDR1	-2.8	C20orf85	-2.8	RBM23	-2.8
CD8B	-2.7	CRISPLD2	-2.8	MAT1A	-2.8	SPN	-2.8
ATP4A	-2.7	PDE4A	-2.8	IRS2	-2.8	IRX6	-2.8
PLXNA4	-2.7	AK094155	-2.8	MYL9	-2.8	DPYSL3	-2.8
SP100	-2.7	C14orf79	-2.8	LPP	-2.8	SEC24C	-2.8
KANK3	-2.7	ZNF445	-2.8	HTR1D	-2.8	LAIR1	-2.8
MFGE8	-2.7	HLA-G	-2.8	GLT25D2	-2.8	CN294989	-2.8
WDR82	-2.7	BC006216	-2.8	MAN2C1	-2.8	SLC9A7	-2.8
TTC4	-2.7	AF090927	-2.8	LOC100506670	-2.8	LTBP3	-2.8
C2orf19	-2.7	FAM47E	-2.8	UBTF	-2.8	LOC158863	-2.8
SUSD5	-2.7	LOC100129434	-2.8	CYP2E1	-2.8	COMP	-2.8
MITF	-2.7	HLA-J	-2.8	WNK2	-2.8	ZNF843	-2.9
THC2608133	-2.7	BCL2L11	-2.8	MRVI1-AS1	-2.8	PIEZO2	-2.9
NDUFV3	-2.7	IRF5	-2.8	DOCK3	-2.8	ZP3	-2.9
FOXI3	-2.7	LMCD1	-2.8	LMOD1	-2.8	LOC401431	-2.9
KRT8P41	-2.7	KIAA0930	-2.8	HLA-E	-2.8	SLC3A2	-2.9
FLJ42627	-2.7	TBX3	-2.8	ENST00000515814	-2.8	ENST00000390319	-2.9
NPIP	-2.7	COL13A1	-2.8	ENST00000431031	-2.8	AMHR2	-2.9

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
DNPEP	-2.9	ACADVL	-2.9	ENST00000452643	-2.9	ELN	-3.0
THC2652093	-2.9	RBM38	-2.9	WFDC5	-2.9	ZNF77	-3.0
KBTBD4	-2.9	ATOH7	-2.9	CLK3	-2.9	ADAMTSL2	-3.0
HSPA6	-2.9	OR1E1	-2.9	TAS2R14	-2.9	HIST1H2BK	-3.0
OR10A2	-2.9	MYO5A	-2.9	C17orf74	-2.9	SERPING1	-3.0
LOC100287482	-2.9	IRX6	-2.9	TNS1	-2.9	ENST00000439298	-3.0
SLC46A1	-2.9	NXF3	-2.9	PCDHGB2	-2.9	CD24	-3.0
UBAP1L	-2.9	CCDC135	-2.9	ABHD1	-2.9	GMDS	-3.0
THC2681839	-2.9	THC2685727	-2.9	THC2719547	-2.9	EWSR1	-3.0
LIFR	-2.9	ENST00000355290	-2.9	NOB1	-2.9	ENST00000453166	-3.0
PCSK6	-2.9	MLXIP	-2.9	EME2	-2.9	THC2647345	-3.0
FLJ39653	-2.9	SYT17	-2.9	MYL3	-2.9	CYP2B6	-3.0
LRRC19	-2.9	EIF4H	-2.9	HSPA8	-2.9	CAMK2D	-3.0
CYP27B1	-2.9	CHST10	-2.9	PHF8	-2.9	CRTC3	-3.0
HSD11B1L	-2.9	ACTBL2	-2.9	AK092508	-2.9	AK023572	-3.0
THC2526765	-2.9	E2F4	-2.9	PPME1	-3.0	ASTN1	-3.0
ANK1	-2.9	DHX58	-2.9	DMD	-3.0	AK000735	-3.0
CLIP4	-2.9	TBC1D3B	-2.9	ZIM2	-3.0	TRPM4	-3.0
AQP7	-2.9	RAPGEF3	-2.9	SPDYE2	-3.0	NKX6-3	-3.0
THC2564488	-2.9	RARA	-2.9	C1orf114	-3.0	SUV420H1	-3.0
VCL	-2.9	DLST	-2.9	CNDP2	-3.0	PCDHB1	-3.0
DUSP2	-2.9	ABCB11	-2.9	AK093006	-3.0	C8orf33	-3.0
SLC43A2	-2.9	WNK4	-2.9	FOXR1	-3.0	LOC157562	-3.0
AK093691	-2.9	ARF1	-2.9	CHAC1	-3.0	KRTAP4-12	-3.0
CA7	-2.9	THC2755341	-2.9	KDR	-3.0	CFD	-3.0
AF264621	-2.9	AK056734	-2.9	PNMAL1	-3.0	ZNRF4	-3.0
CLYBL	-2.9	ACTC1	-2.9	VIL1	-3.0	PGS1	-3.0
HRK	-2.9	PRM1	-2.9	ENST00000444164	-3.0	MALAT1	-3.0
LOC100505974	-2.9	PITPNM2	-2.9	AQP3	-3.0	PSORS1C2	-3.0
PRDM15	-2.9	NOL6	-2.9	ACTA2	-3.0	UBTF	-3.0
THC2660977	-2.9	TTLL11	-2.9	OR7E91P	-3.0	ZNF586	-3.0
CYP4V2	-2.9	MBTPS1	-2.9	PRODH	-3.0	SCHIP1	-3.0
FLJ33360	-2.9	ARF1	-2.9	TRAFD1	-3.0	OSTalpha	-3.0
THC2698927	-2.9	PDE9A	-2.9	PTGER1	-3.0	BCL2L11	-3.0
RHOB	-2.9	ZMAT3	-2.9	KIAA0913	-3.0	FBXO8	-3.0
C14orf79	-2.9	MYL5	-2.9	MINA	-3.0	AF088007	-3.0
XBP1	-2.9	MAGEC2	-2.9	LOC100287723	-3.0	CRLF1	-3.0
ASB13	-2.9	GPR97	-2.9	THC2570021	-3.0	CEP97	-3.0
DA438590	-2.9	GPD1	-2.9	HTR1A	-3.0	ZNF79	-3.0
GLA	-2.9	MAP1LC3A	-2.9	CD276	-3.0	MUC20	-3.0
JPH3	-2.9	COX7A1	-2.9	BC013933	-3.0	PCNXL2	-3.0

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
BE184907	-3.0	BX485389	-3.1	NUP98	-3.1	THC2521437	-3.1
GPR17	-3.0	C9orf3	-3.1	AF187554	-3.1	ZNF341	-3.1
TRPM3	-3.0	FNDC4	-3.1	THC2700488	-3.1	SRCRB4D	-3.1
FOLR3	-3.0	LOC100506990	-3.1	THC2690323	-3.1	NCOA7	-3.1
BC031954	-3.0	HTRA1	-3.1	POM121	-3.1	HSPA1A	-3.1
THC2529512	-3.0	FLJ23867	-3.1	CAPN8	-3.1	RBP1	-3.1
ASMTL	-3.0	TTC17	-3.1	IGFBP6	-3.1	LOC645752	-3.1
ACAN	-3.0	CCDC88C	-3.1	ENST00000390252	-3.1	PRB4	-3.1
ENST00000390381	-3.0	DLG4	-3.1	KCNT1	-3.1	ADCY1	-3.2
BPTF	-3.0	GUSBP10	-3.1	THC2777514	-3.1	LPA	-3.2
ABCA7	-3.0	TSTD1	-3.1	CACNB2	-3.1	THC2481344	-3.2
CACNA1B	-3.0	AKAP4	-3.1	AF086013	-3.1	BC031973	-3.2
ENST00000504184	-3.0	CLDN15	-3.1	AK026675	-3.1	CAMTA1	-3.2
ALOXE3	-3.0	IFI6	-3.1	IL18BP	-3.1	PNOC	-3.2
ADAMTS13	-3.0	LOC100506478	-3.1	TBX3	-3.1	C22orf23	-3.2
CDH18	-3.0	TUSC5	-3.1	POTEE	-3.1	RYR1	-3.2
CRYBA4	-3.0	CARKD	-3.1	SARDH	-3.1	LGMN	-3.2
SENP6	-3.0	MYBPC3	-3.1	LRPAP1	-3.1	CYB561D1	-3.2
BX119880	-3.0	LOC100133091	-3.1	MORC4	-3.1	AK124281	-3.2
NFRKB	-3.0	ENST00000433600	-3.1	FPGS	-3.1	FHIT	-3.2
CCL19	-3.0	DOLPP1	-3.1	LOXL4	-3.1	TBC1D25	-3.2
H2AFB2	-3.0	SYNJ2	-3.1	LOC100132147	-3.1	TMEM217	-3.2
USHBP1	-3.0	BCL7B	-3.1	SLC7A5	-3.1	THC2757796	-3.2
BZRAP1	-3.0	GPCPD1	-3.1	GTF2IRD2B	-3.1	POTEM	-3.2
PCCB	-3.0	TCEAL7	-3.1	PTK6	-3.1	LOC388796	-3.2
AI247465	-3.0	KIAA0513	-3.1	AA158952	-3.1	CU690321	-3.2
IDI2	-3.0	PRMT5	-3.1	RDM1	-3.1	SHBG	-3.2
GOLM1	-3.0	C8orf33	-3.1	IRS1	-3.1	RBMS1	-3.2
LRFN2	-3.0	ABCF2	-3.1	GANAB	-3.1	CTSB	-3.2
LAMB1	-3.0	HSD17B8	-3.1	INO80D	-3.1	ENST00000434871	-3.2
LOC100132167	-3.0	NOXO1	-3.1	ENST00000428471	-3.1	PGM5	-3.2
CFHR3	-3.0	LMX1A	-3.1	RHOH	-3.1	C10orf25	-3.2
C1orf228	-3.0	HNF1B	-3.1	CFH	-3.1	SYNGR2	-3.2
BF210146	-3.0	MLLT4	-3.1	SLC25A30	-3.1	CARD18	-3.2
VPS26B	-3.1	THC2638238	-3.1	CD83	-3.1	COX19	-3.2
ARSG	-3.1	IL1F10	-3.1	CCNY	-3.1	LINC00085	-3.2
EIF3F	-3.1	ATF5	-3.1	CCDC88C	-3.1	HAPLN4	-3.2
THC2536659	-3.1	PYGM	-3.1	IYD	-3.1	SPECC1	-3.2
U79293	-3.1	CNN1	-3.1	EDN2	-3.1	LOC100653030	-3.2
FGF7	-3.1	BC009036	-3.1	RPA4	-3.1	PPP1R3F	-3.2
C14orf81	-3.1	USP41	-3.1	TMEM185B	-3.1	LOC96610	-3.2

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ZMIZ2	-3.2	THC2713078	-3.3	NRN1	-3.3	GIGYF2	-3.4
GBA2	-3.2	SLC22A16	-3.3	THC2654595	-3.3	AHNAK	-3.4
MALAT1	-3.2	AK124841	-3.3	AKAP12	-3.3	TMEM174	-3.4
LOC440792	-3.2	TGFBI	-3.3	LIF	-3.3	THC2679528	-3.4
COL6A2	-3.2	THSD4	-3.3	COL11A2	-3.3	GUCA1B	-3.4
KRTAP1-1	-3.2	CLU	-3.3	ENST00000398878	-3.3	AL844324	-3.4
TSGA10	-3.2	FLJ36116	-3.3	PROKR2	-3.3	PLK5	-3.4
OR10T2	-3.2	MEF2BNB-MEF2B	-3.3	AHNAK2	-3.3	SLC34A1	-3.4
RCN3	-3.2	TMEM38A	-3.3	SLC9A2	-3.3	DRD5	-3.4
CELF4	-3.2	AF321778	-3.3	RASA4	-3.3	MPV17L	-3.4
HLA-DMB	-3.2	LOC338620	-3.3	BCHE	-3.3	LOC100505880	-3.4
SAMD9L	-3.2	TMEM25	-3.3	NGF	-3.3	CHRD	-3.4
CFH	-3.2	ACTB	-3.3	TBC1D10C	-3.3	AF161340	-3.4
CNN2	-3.2	COLQ	-3.3	PLXNA3	-3.3	KANSL3	-3.4
TOM1L2	-3.2	POTEF	-3.3	ENST00000354689	-3.3	THC2615996	-3.4
ENST00000421735	-3.2	PTGDS	-3.3	PLA2G2F	-3.3	YARS	-3.4
LOC100506571	-3.2	ATP8B3	-3.3	AF289615	-3.3	HRASLS2	-3.4
KIAA1984	-3.2	ENST00000532936	-3.3	MALAT1	-3.3	INPP1	-3.4
TAPBPL	-3.2	SPDYE7P	-3.3	CPXM1	-3.3	WNT10A	-3.4
MIF4GD	-3.2	THC2748290	-3.3	LENG8	-3.3	CES3	-3.4
PRSS1	-3.2	TRIB3	-3.3	ZDHHC9	-3.3	CHRM3	-3.4
ENST00000414210	-3.2	DRP2	-3.3	PIK3IP1	-3.3	HIPK2	-3.4
PP14571	-3.2	THC2544198	-3.3	PARVG	-3.3	MUC6	-3.4
CFH	-3.2	MPO	-3.3	RALGDS	-3.3	VPS13C	-3.4
HLA-C	-3.2	C16orf7	-3.3	TNF	-3.3	PDXDC2P	-3.4
ANKRD11	-3.2	SERPINB8	-3.3	CDK9	-3.3	C14orf79	-3.4
PLXDC1	-3.2	IDUA	-3.3	ADAP2	-3.3	THC2503819	-3.4
HM358951	-3.2	CPXM2	-3.3	HSD17B14	-3.3	FLJ38576	-3.4
CDH23	-3.2	AGPAT3	-3.3	EXT1	-3.3	NOL6	-3.4
CNTF	-3.2	THC2689802	-3.3	CACNA1B	-3.4	THC2680634	-3.4
LPP	-3.2	KCNQ2	-3.3	LOC497257	-3.4	RASSF8	-3.4
FXYD6	-3.2	RBMS1	-3.3	THC2622086	-3.4	CR1	-3.4
ZNF79	-3.2	ENST00000541329	-3.3	GPR155	-3.4	INO80	-3.4
PVRL3	-3.2	RCN1	-3.3	ZNF577	-3.4	LAT2	-3.4
CNKSR1	-3.2	NID1	-3.3	THC2727290	-3.4	NDUFA10	-3.4
A4GALT	-3.2	RSPH9	-3.3	CASQ1	-3.4	CYFIP2	-3.4
EXT1	-3.3	ASS1	-3.3	SULF2	-3.4	CR2	-3.4
PPAN-P2RY11	-3.3	TSPAN33	-3.3	SH3BP5	-3.4	BTG2	-3.4
C8orf60	-3.3	TSHZ1	-3.3	GCLM	-3.4	PLEKHA5	-3.4
SPTBN1	-3.3	TACR2	-3.3	OCM2	-3.4	FAM95B1	-3.4
PCGF5	-3.3	AK024602	-3.3	SLC45A4	-3.4	IRAK1	-3.4

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ZC3H10	-3.4	LAMP3	-3.5	LPP	-3.6	DDX31	-3.6
MYO15A	-3.4	FCGRT	-3.5	NEFM	-3.6	ZNF552	-3.6
SLC16A14	-3.4	HLA-DPB1	-3.5	ENST00000426099	-3.6	BX537819	-3.7
MMP14	-3.4	NLRP1	-3.5	INPP5D	-3.6	SQSTM1	-3.7
MALAT1	-3.4	BC001335	-3.5	CNN2	-3.6	SSTR5	-3.7
HGFAC	-3.4	CARS	-3.5	AK091914	-3.6	CU676313	-3.7
LOC100130331	-3.4	AL832534	-3.5	ATP8B3	-3.6	TREML1	-3.7
GALNT9	-3.4	EFHB	-3.5	OVGP1	-3.6	LINC00256B	-3.7
LOC100133050	-3.4	BC033539	-3.5	ENST00000531225	-3.6	KIAA1755	-3.7
NDP	-3.4	LOC100507022	-3.5	BAGE4	-3.6	NPR3	-3.7
CU692385	-3.5	SPATA13	-3.5	CEACAM19	-3.6	TBC1D9	-3.7
AK024382	-3.5	UCN3	-3.5	FOXA3	-3.6	PADI4	-3.7
THC2650352	-3.5	BEND7	-3.5	OR7E91P	-3.6	PTGFRN	-3.7
PLAC1	-3.5	MAG	-3.5	CTSS	-3.6	MICAL2	-3.7
IGF2	-3.5	CBX6	-3.5	NFATC1	-3.6	BRD2	-3.7
C17orf99	-3.5	THC2729353	-3.5	DOCK8	-3.6	LIPF	-3.7
FOXJ1	-3.5	NPHS1	-3.5	ANKRD20A2	-3.6	ENST00000505712	-3.7
ANKDD1A	-3.5	GPR35	-3.5	OXCT2	-3.6	HLA-B	-3.7
LOC100505915	-3.5	CLCNKA	-3.5	MUC5AC	-3.6	NEFH	-3.7
MFGE8	-3.5	TLE6	-3.5	TM4SF1	-3.6	PSAP	-3.7
LOC100128922	-3.5	GCLM	-3.5	CCNT1	-3.6	UCA1	-3.7
AK027225	-3.5	BRF2	-3.5	NOTCH2	-3.6	EEF1A2	-3.7
COL23A1	-3.5	THC2708422	-3.5	AF075112	-3.6	NPM2	-3.7
HYAL1	-3.5	MUC2	-3.5	PRKCA	-3.6	BC001335	-3.7
FAM129C	-3.5	RFPL2	-3.5	AXDND1	-3.6	ARMC5	-3.7
UTP14A	-3.5	GJC2	-3.5	LOC100507780	-3.6	CBX4	-3.7
RASGRP1	-3.5	FLRT3	-3.5	IGFBP4	-3.6	GPR172B	-3.7
HLA-B	-3.5	MYPN	-3.5	COL3A1	-3.6	SLC1A4	-3.7
PRKAB1	-3.5	METTL16	-3.5	THC2591546	-3.6	CRYM	-3.7
TMEM130	-3.5	CCDC113	-3.5	TRAPPC6A	-3.6	SMPDL3B	-3.7
BC034930	-3.5	AK124352	-3.5	PLK3	-3.6	ELF3	-3.7
NOTCH1	-3.5	HLA-B	-3.5	CSTA	-3.6	SCRT1	-3.7
SEL1L3	-3.5	FERMT3	-3.5	FCGBP	-3.6	FIGF	-3.7
THC2690657	-3.5	POM121L8P	-3.5	SLC2A13	-3.6	C1orf114	-3.7
CRIP1	-3.5	ENST00000428709	-3.5	USP46	-3.6	AF471454	-3.7
MGC16275	-3.5	ENST00000399269	-3.6	RASGRP1	-3.6	ST6GALNAC2	-3.7
IL1R1	-3.5	ENST00000415530	-3.6	CNTNAP3	-3.6	BEST3	-3.7
AHNAK	-3.5	HSPA1A	-3.6	BC034271	-3.6	SYNJ2	-3.7
POM121L1P	-3.5	C2orf73	-3.6	MIR22HG	-3.6	TGM7	-3.7
ENST00000448014	-3.5	ATP10A	-3.6	C3orf20	-3.6	AGTR1	-3.7
AFAP1-AS1	-3.5	TPM1	-3.6	FNDC3B	-3.6	ENST00000321930	-3.7

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
THC2710703	-3.7	CYFIP2	-3.8	PKP1	-3.9	MALAT1	-4.0
THC2532114	-3.7	AK022044	-3.8	RNF125	-3.9	SLC22A23	-4.0
CD163L1	-3.7	RPL23AP32	-3.8	AEN	-3.9	TFPI	-4.0
EPPK1	-3.7	ANKRD20A5P	-3.8	CEBPB	-3.9	SLC25A25	-4.0
CROCCP3	-3.7	ABCA6	-3.8	BM913108	-3.9	MADCAM1	-4.0
SLITRK2	-3.7	IGSF3	-3.8	PGCP	-3.9	NT5DC3	-4.0
RNASET2	-3.7	HLA-E	-3.8	ACSS1	-3.9	ITIH6	-4.0
LOC100500938	-3.7	PDLIM5	-3.8	NAV2	-3.9	YPEL2	-4.0
RND1	-3.7	FAM83F	-3.8	INHBA	-3.9	SERPINA3	-4.0
AKAP8L	-3.7	GLIPR1	-3.8	TAF7L	-3.9	GRIP2	-4.0
DNAH12	-3.7	WIPF3	-3.8	X01147	-3.9	WDR1	-4.0
DKFZP434K028	-3.7	THC2678309	-3.8	BRS3	-3.9	TM7SF2	-4.0
TPM1	-3.7	LOC399851	-3.9	BIRC3	-3.9	LOC100653060	-4.0
ISM2	-3.7	THC2680414	-3.9	NP110384	-3.9	HLA-C	-4.0
C20orf196	-3.8	ERO1LB	-3.9	LINC00256A	-3.9	LOC100128644	-4.0
SLC7A5	-3.8	BC042064	-3.9	AF257098	-3.9	RHPN1	-4.0
N4BP2L2	-3.8	TMEM190	-3.9	MYCT1	-3.9	FGL1	-4.0
SPAG4	-3.8	SLITRK4	-3.9	KLHL4	-3.9	LOC339290	-4.0
PPM1J	-3.8	OLFML3	-3.9	MGC23284	-3.9	ATF3	-4.0
FBN2	-3.8	HLA-DOA	-3.9	H2BFXP	-3.9	AF116684	-4.0
GALNT10	-3.8	AK021593	-3.9	NEAT1	-3.9	TRIM50	-4.0
SRXN1	-3.8	ENST00000424931	-3.9	TMEM59L	-3.9	BX105278	-4.0
ASMTL	-3.8	VSTM2L	-3.9	TNC	-3.9	AK097045	-4.0
PON1	-3.8	AOC3	-3.9	JAKMIP1	-3.9	FBXL7	-4.0
USH1C	-3.8	PDLIM5	-3.9	ENST00000537552	-3.9	IGF2	-4.0
THC2520478	-3.8	FAM132A	-3.9	FAM71F1	-3.9	HEPACAM2	-4.0
BF207040	-3.8	LRRC41	-3.9	SCUBE2	-4.0	AK092921	-4.0
CRYL1	-3.8	SPATA13	-3.9	BX094982	-4.0	MST1	-4.0
NOXA1	-3.8	THC2500237	-3.9	ADAMTSL4	-4.0	AY946020	-4.0
SLC2A4	-3.8	COL13A1	-3.9	COL6A2	-4.0	LOC148709	-4.1
MFNG	-3.8	NECAP1	-3.9	FOSL1	-4.0	CT45A1	-4.1
CCNB2	-3.8	MIR137HG	-3.9	BM666601	-4.0	PVR	-4.1
POTEKP	-3.8	AK054562	-3.9	LRG1	-4.0	DCAKD	-4.1
ZBTB12	-3.8	NPIP	-3.9	HLA-F	-4.0	EPHA2	-4.1
CCR3	-3.8	SLC22A18	-3.9	HLA-A	-4.0	SIRPA	-4.1
BGN	-3.8	CNKSR3	-3.9	TDRD10	-4.0	LOC283174	-4.1
ENST00000390597	-3.8	KCTD12	-3.9	ENST00000538795	-4.0	LPP	-4.1
GABRA3	-3.8	OR51B5	-3.9	CEACAM21	-4.0	AF222023	-4.1
BC071773	-3.8	GAGE3	-3.9	LGI2	-4.0	VTI1A	-4.1
PTPRN	-3.8	ENST00000517658	-3.9	CAMK1D	-4.0	ENST00000321800	-4.1
SCN5A	-3.8	RTP1	-3.9	ELANE	-4.0	XM_003118965	-4.1

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
FAM196A	-4.1	THC2515402	-4.2	MMEL1	-4.3	LOC100131170	-4.5
PKLR	-4.1	PLEKHB1	-4.2	GRIN2C	-4.3	FGF21	-4.5
MUC3A	-4.1	HOXB13	-4.2	HLA-A	-4.3	SLC22A18	-4.6
TTYH2	-4.1	AHNAK	-4.2	MUC3	-4.3	MYOZ3	-4.6
ENST00000356370	-4.1	ADM	-4.2	GAS6	-4.3	STRC	-4.6
AJ004954	-4.1	SLC39A11	-4.2	RFPL1	-4.3	TM7SF2	-4.6
LOC100287482	-4.1	AK027091	-4.2	CRYBA2	-4.4	THEG	-4.6
FOLR1	-4.1	GADD45A	-4.2	NETO2	-4.4	NTN5	-4.6
CRY2	-4.1	CN480368	-4.2	ZDHHC14	-4.4	TSPAN15	-4.6
MYL4	-4.1	ENST00000427392	-4.2	BC019703	-4.4	POU5F1	-4.6
GABRQ	-4.1	ENST00000553155	-4.2	TSNARE1	-4.4	ARC	-4.6
PRNT	-4.1	GRIK3	-4.2	MTHFD2L	-4.4	PCDHB9	-4.6
ADARB1	-4.1	WDR33	-4.2	PLN	-4.4	PPIC	-4.6
OPCML	-4.1	SESN2	-4.2	ENST00000397549	-4.4	NPVF	-4.6
PRDM11	-4.1	TRPV2	-4.2	TRH	-4.4	LARP1	-4.6
DDIT4	-4.1	CXCL3	-4.2	DDI2	-4.4	SSX3	-4.6
ACSS2	-4.1	TTBK2	-4.2	MST1P2	-4.4	MGC23270	-4.6
THC2679528	-4.1	BRD4	-4.2	MAFIP	-4.4	EOMES	-4.6
HLA-H	-4.1	FGF7	-4.3	GSN	-4.4	THC2676635	-4.6
AK055679	-4.1	CPA5	-4.3	LANCL2	-4.4	AK021777	-4.6
SULT2B1	-4.1	LOXL4	-4.3	CTNNA3	-4.4	LPP	-4.6
PARM1	-4.1	WDR1	-4.3	EBF2	-4.4	THC2643739	-4.6
HLA-B	-4.1	SERPINF1	-4.3	DNAH12	-4.4	MIR22HG	-4.7
KIAA1751	-4.1	COL7A1	-4.3	CLDN18	-4.4	MANSC1	-4.7
ENST00000333156	-4.1	LAT2	-4.3	THC2677796	-4.4	MAFIP	-4.7
UBL4B	-4.1	TXLNA	-4.3	AK091308	-4.4	BX119882	-4.7
SVOPL	-4.1	TESC	-4.3	SLC3A2	-4.4	BCO2	-4.7
BTBD9	-4.2	ECEL1	-4.3	HUS1B	-4.4	ENST00000542270	-4.7
ARNT2	-4.2	PVR	-4.3	ACSM3	-4.5	NFYA	-4.7
CBX6	-4.2	F10	-4.3	BX537816	-4.5	HLA-DMB	-4.7
AM181370	-4.2	S73202	-4.3	PTPRR	-4.5	BST2	-4.7
ZYX	-4.2	BC018589	-4.3	ATP10A	-4.5	CYP11B1	-4.7
PLEKHB1	-4.2	PPIC	-4.3	AV756170	-4.5	LOC151009	-4.7
CCR7	-4.2	THC2741548	-4.3	SPACA3	-4.5	C15orf50	-4.7
CA945082	-4.2	HLA-C	-4.3	TSPAN33	-4.5	BX106493	-4.7
CELA1	-4.2	CHST9	-4.3	TPM1	-4.5	ENST00000446232	-4.7
CLSTN3	-4.2	L12052	-4.3	B3GNT9	-4.5	THC2535753	-4.7
HIVEP3	-4.2	HLA-L	-4.3	RBM38	-4.5	IL21	-4.7
LONRF2	-4.2	SOCS3	-4.3	AY227436	-4.5	CLTB	-4.7
THC2681829	-4.2	OR5H1	-4.3	NP414419	-4.5	LOC727982	-4.7
KLHL4	-4.2	HUS1B	-4.3	KCNA10	-4.5	SLC43A2	-4.7

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
LRRC47	-4.7	COLEC10	-5.0	THC2728374	-5.2	NP450512	-5.6
ADARB2	-4.7	XCL2	-5.0	MAGEC1	-5.3	ANXA8L2	-5.6
ENST00000390243	-4.7	NLRP12	-5.0	FAM74A1	-5.3	BC033227	-5.6
AKAP12	-4.8	LOC349196	-5.0	BI828537	-5.3	RNASE4	-5.6
TMCC2	-4.8	MUC5B	-5.0	NETO2	-5.3	AK054921	-5.6
CD59	-4.8	SPRR2C	-5.0	FER1L4	-5.3	CX3CL1	-5.6
PMEL	-4.8	KCNV2	-5.0	ERP27	-5.3	THC2624360	-5.6
OR51A7	-4.8	LOC157627	-5.0	CCDC144A	-5.3	CU690251	-5.6
ENST00000519648	-4.8	CBFA2T3	-5.0	LTBP2	-5.3	ENST00000390636	-5.7
THC2653489	-4.8	SH2D3C	-5.0	TRIOBP	-5.3	TTYH2	-5.7
AGPAT9	-4.8	OR6Y1	-5.0	PPP1R1A	-5.3	ICAM4	-5.7
MAB21L1	-4.8	SPP1	-5.0	ENST00000390323	-5.3	GATA5	-5.7
BC012753	-4.8	CELF6	-5.1	SAT1	-5.3	GAGE7	-5.7
THC2560073	-4.8	AF116619	-5.1	PAX4	-5.3	ENST00000369158	-5.7
NTSR2	-4.8	OTOA	-5.1	GPR98	-5.3	GNAZ	-5.7
MYO1G	-4.8	NPFFR2	-5.1	CD52	-5.3	AK026965	-5.7
ZNF263	-4.8	SRGAP1	-5.1	EEF1D	-5.3	PLXDC1	-5.7
SCNN1A	-4.9	TCTE3	-5.1	THSD4	-5.3	NLRP12	-5.7
ADAMTS9-AS2	-4.9	RNF157	-5.1	IL6R	-5.4	THC2653997	-5.7
SAT1	-4.9	HLA-H	-5.1	THC2651324	-5.4	CNTNAP3B	-5.7
ART5	-4.9	SLC7A11	-5.1	LOC339240	-5.4	THC2699065	-5.7
PRSS47	-4.9	ZDHHC22	-5.1	SPDYE8P	-5.4	NP111779	-5.8
IL1RAP	-4.9	MYO3B	-5.1	LIPG	-5.4	HIF3A	-5.8
HLA-A	-4.9	LOC729652	-5.1	TNFRSF10D	-5.4	ENST00000443771	-5.8
BTN3A1	-4.9	ATP1B2	-5.1	THC2655842	-5.4	ANG	-5.8
DICER1-AS	-4.9	GPR160	-5.1	TPD52L1	-5.4	IFI16	-5.8
ARAP3	-4.9	THC2707266	-5.1	FEZ1	-5.4	IGLON5	-5.8
ENST00000440200	-4.9	SRGN	-5.1	GOLGA6L6	-5.4	ENST00000417781	-5.8
FLJ31485	-4.9	FCRL3	-5.1	LOC339240	-5.4	RUFY2	-5.8
NRP1	-4.9	KIR2DS4	-5.1	AKAP12	-5.5	ENST00000506492	-5.8
RELB	-4.9	MYO15A	-5.2	DNAH1	-5.5	CHODL	-5.9
THAP7-AS1	-4.9	MYO1E	-5.2	STC2	-5.5	ANXA10	-5.9
CCKBR	-5.0	ZNF503	-5.2	THC2753968	-5.5	HSF2BP	-5.9
NACAD	-5.0	TSC22D3	-5.2	THC2662725	-5.5	MANEAL	-5.9
SHANK1	-5.0	CYP7B1	-5.2	COL5A1	-5.5	LGALS12	-5.9
GAL3ST1	-5.0	ABTB2	-5.2	THC2487011	-5.5	ARPC4-TTLL3	-5.9
PLXND1	-5.0	RGS9	-5.2	TNFSF15	-5.5	AF119913	-5.9
PIP5KL1	-5.0	ENST00000544461	-5.2	DNALI1	-5.5	ABAT	-5.9
CEBPA	-5.0	DKKL1	-5.2	CPLX3	-5.5	THC2701140	-5.9
LY6G5C	-5.0	TP53AIP1	-5.2	THC2738878	-5.6	UPK1A	-5.9
C9orf131	-5.0	CCDC153	-5.2	KIAA1217	-5.6	FLJ41350	-5.9

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
AI911586	-5.9	SLC16A14	-6.5	C7orf69	-7.3	RASD2	-8.6
PPM1E	-6.0	RGMA	-6.5	BEST1	-7.3	GLYAT	-8.6
GPHA2	-6.0	EXD3	-6.5	TNFRSF11B	-7.3	TNFAIP8L3	-8.6
OR4S1	-6.0	SORBS2	-6.5	SQRDL	-7.3	VLDLR	-8.7
DHDH	-6.0	TDRD10	-6.5	GLB1L2	-7.4	GDF15	-8.7
AF010144	-6.0	NGFR	-6.5	FAM149A	-7.4	DQ786230	-8.7
CFI	-6.0	AMZ2P1	-6.6	GABARAPL3	-7.4	PDE11A	-8.8
CNTNAP3	-6.0	LAMA2	-6.6	TNFRSF11B	-7.4	SLC7A11	-8.8
U94903	-6.1	AI732190	-6.6	SPAG9	-7.4	GABARAPL1	-8.8
THC2654921	-6.1	CSAG1	-6.6	ENST00000361201	-7.5	NPY1R	-8.9
THC2740861	-6.1	CDK6	-6.6	POSTN	-7.5	FUT1	-9.0
NR4A2	-6.1	BF983943	-6.6	RBFOX1	-7.5	GNG13	-9.0
AF007193	-6.1	PFKFB3	-6.6	GDAP1L1	-7.5	BX091616	-9.0
REXO1L1	-6.1	TBX6	-6.7	HES2	-7.6	HLA-DMA	-9.1
ZBTB34	-6.1	SERPINA10	-6.7	BX114143	-7.6	GPR64	-9.2
LOC400794	-6.1	XKR4	-6.7	RHCE	-7.6	ABCB4	-9.3
ENST00000390539	-6.1	SIRPG	-6.7	FOXD4	-7.7	HTRA3	-9.3
SLC16A6	-6.1	ITGBL1	-6.7	FAM19A4	-7.7	THC2685688	-9.5
PI16	-6.1	ITGA1	-6.7	PDE11A	-7.7	PTPRJ	-9.5
RBPJL	-6.2	P2RX1	-6.8	USP6	-7.7	FAM149A	-9.5
LIPG	-6.2	THC2653283	-6.8	MAP3K5	-7.7	TSPAN32	-9.5
SLC2A13	-6.2	C9orf47	-6.8	SOD3	-7.9	ABP1	-9.6
PDGFA	-6.2	TJP3	-6.9	SLC16A6	-7.9	AW627629	-9.7
FBLN2	-6.3	SLC30A8	-6.9	MIR7-3HG	-7.9	LBX1	-9.7
COX6B2	-6.3	TCF23	-6.9	ENST00000377186	-8.0	KIAA1751	-9.7
BC029452	-6.3	TLR3	-6.9	DLX3	-8.0	THC2636529	-9.8
ATF3	-6.3	ACTG2	-7.0	KLK8	-8.0	LY9	-9.8
U88896	-6.3	TAS2R19	-7.0	BQ674642	-8.0	PLA2G16	-9.9
NDUFA10	-6.3	NPHS2	-7.1	EPPK1	-8.0	CLDN1	-10.0
LDHD	-6.3	ENST00000443034	-7.1	THC2712710	-8.0	KLHL6	-10.1
C15orf2	-6.3	CREB3L3	-7.1	FAM153A	-8.1	CDKN1A	-10.1
SPOCK3	-6.4	TEX14	-7.1	PRINS	-8.2	THC2687042	-10.1
FOSL1	-6.4	PDE11A	-7.1	THC2712687	-8.2	PLXNA1	-10.2
LPP	-6.4	UPK3A	-7.1	SLC27A2	-8.2	CT45A5	-10.3
GPR56	-6.4	SYCE3	-7.1	OSGIN1	-8.2	ENST00000518339	-10.3
CPA2	-6.4	BX112754	-7.2	CX165016	-8.3	CASC2	-10.3
CEBPA	-6.4	ENST00000439259	-7.2	D16474	-8.3	PLK2	-10.3
IRS1	-6.4	LOC100652749	-7.2	PLVAP	-8.3	STC2	-10.3
PRAMEF8	-6.5	IFI16	-7.2	KCNK10	-8.4	ALDH1L1	-10.4
AL137705	-6.5	NRG2	-7.2	NRG1	-8.5	NKX2-5	-10.4
SELENBP1	-6.5	GABARAPL1	-7.3	LINC00301	-8.5	THC2726661	-10.5

Appendix VI Gene Expression Changes in $A2780_{DXL-CC}$ vs. $A2780_{DXL}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
PIK3R3	-10.5	C13orf15	-18.4				
LOC284561	-10.6	THC2693741	-18.5				
FAM46A	-10.6	MAOB	-19.1				
MYO6	-10.6	MYH11	-19.9				
F7	-10.7	TNFSF10	-21.4				
LRRK2	-10.7	EPHB6	-21.6				
THC2686110	-10.8	COL20A1	-21.6				
C8orf85	-10.9	MAOB	-22.1				
MYO6	-10.9	FAM74A3	-22.2				
NPFFR2	-11.0	MAL2	-22.7				
SSPO	-11.0	ANXA1	-23.1				
CAMK4	-11.2	MYH11	-23.5				
C4orf49	-11.3	ARHGAP9	-26.9				
ENST00000538912	-11.6	FGF18	-29.3				
LEPREL1	-11.8	AGTR1	-29.9				
MEGF11	-12.0	AK094603	-30.1				
HOXA2	-12.2	TMEFF2	-34.0				
IL3RA	-12.2	SORBS2	-35.0				
LOC283454	-12.7	ALDH1A1	-39.0				
C13orf15	-12.9	FGF18	-42.2				
FBN2	-13.0	THC2682885	-69.1				
SLC1A4	-13.0	SORBS2	-69.1				
BM926140	-13.1	TSLP	-276				
MB	-13.3						
KCNE1	-13.5						
AL834280	-13.7						
JAKMIP3	-13.8						
CNR1	-14.4						
CDKN1A	-14.4						
BX090929	-14.5						
HLA-DMA	-14.5						
ABCB1	-14.7						
THC2661509	-14.8						
HMOX1	-14.8						
SPINK2	-15.1						
ENST00000318245	-15.9						
HMCN1	-16.0						
SLITRK3	-16.1						
NKX2-1	-16.2						
CER1	-16.8						
TMEM232	-17.7						

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
L1TD1	897.8	PDE1A	74.6	C7orf58	33.6	STAMBPL1	17.2
LAYN	706.3	ELF4	72.7	FGF20	33.6	TNFRSF14	17.2
HSD17B12	385.9	DSEL	69.5	NRXN1	33.2	CD40	17.1
PPP1R1C	373.8	SLC8A1	68.4	IFI27	32.4	PRTFDC1	17.0
FLRT3	373.3	BN2	65.5	NFE2	31.9	NLRC5	16.8
ZFP42	339.5	SLC8A1	65.4	LIN28A	31.2	TRIM56	16.8
BST2	316.4	ONECUT1	65.3	POU1F1	30.9	ENO2	16.8
MEF2C	308.8	RSPO2	60.8	DSEL	29.8	SIX6	16.8
IRX3	297.2	SL1	59.1	FIGN	29.7	C8orf48	16.8
PHOX2B	268.9	S100A11	58.6	KLHDC8A	28.7	FZD8	16.7
AK129542	253.8	NRXN1	56.6	IFNG	28.4	HSD17B12	16.7
APOL6	250.3	ADAMTS5	55.7	IFI27	27.8	TLX3	16.5
IRX5	220.8	ARHGAP28	54.2	FGF18	27.5	ASXL3	16.5
MGP	216.8	AGT	53.1	ALX1	27.4	KBTBD10	16.5
PITX2	215.8	KLHL14	53.0	LOC100144602	27.3	S100A11	16.4
PDE1A	194.8	KANK4	53.0	PDGFC	27.1	IGFBP2	16.1
SUN3	180.3	TNFRSF19	51.4	SOX2	26.9	BE904671	16.1
DLK1	179.1	OC284244	51.0	NKX2-1	26.8	CAV1	15.8
PCDH9	177.6	COL11A1	50.9	METTL7A	26.3	SEMA6A	15.8
GPR158	170.6	NST00000507916	50.8	TRPS1	26.2	NTNG1	15.8
ENST00000555442	166.6	CYB5R2	49.6	CASP1	24.9	ITGA1	15.4
FOXP2	159.8	PDE1A	49.6	THC2628387	24.6	CPA2	15.2
TES	145.5	SAA2	48.9	GRIA3	24.5	ARHGDIB	15.1
HSPA1A	125.8	BHLHE41	48.2	NETO1	24.3	ANKRD22	15.1
C18orf34	124.5	SLC27A6	46.8	PTH2	24.0	PRKCH	15.1
AGMO	117.8	APLN1	46.7	APOL3	23.8	DCDC5	15.1
SAA1	111.5	SEMA3D	46.5	DIRAS3	23.3	SNCG	14.9
NLGN4Y	111.3	BM989848	46.5	ENST00000428928	23.3	A_32_P9737	14.8
ARHGAP28	109.2	GSG1	44.1	DIO3	23.1	FGF18	14.7
XIRP2	100.8	DC2	43.7	MT1F	22.8	RBPMS	14.6
HAND2	100.1	EPHA7	41.5	P2RY2	22.5	GIMAP2	14.6
RSPO2	96.9	LRRC55	41.2	CTNNA2	22.4	CTSF	14.6
ENST00000514673	92.1	TES	40.7	RNLS	21.9	PDE1A	14.6
ASXL3	92.1	MUC15	40.6	TMEM30B	21.0	PCDH19	14.4
RBPMS	92.0	THC2664860	40.4	KANK1	21.0	MBD2	14.3
OTOL1	82.4	CRNDE	39.7	CBR3	19.6	HTR1F	13.9
PPP1R1C	81.4	KITLG	37.1	ABCB1	19.4	XAF1	13.9
PDGFRA	80.5	C11orf88	37.0	IL7	19.2	DDX60	13.9
NLGN4X	76.9	NAV3	36.2	ELF3	18.5	HOXB5	13.8
VAV3	76.1	LIMCH1	35.5	JAG1	18.5	RASGRP2	13.6
SLC15A3	75.6	SFTA3	35.2	A_32_P191141	17.3	LMO1	13.6

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SORT1	13.2	GBP7	10.3	SEMA3E	8.9	AK093713	7.5
MSX1	13.0	MSX1	10.3	BX107298	8.8	MYH11	7.5
BAMBI	12.9	SIPA1	10.3	C1orf198	8.8	MDK	7.4
C7orf58	12.8	SOX6	10.3	CITED2	8.7	WNT3A	7.4
IFIH1	12.8	UBA7	10.2	GBP3	8.7	DKK2	7.4
CDH2	12.7	AK022020	10.2	MX1	8.6	BATF2	7.4
THC2645398	12.6	PYGM	10.1	PLA2G16	8.6	PPP2R2B	7.4
THC2637568	12.5	GBP4	10.1	FAM113B	8.6	NLGN3	7.4
SEMA6D	12.0	PCDH20	10.1	EPHA7	8.6	NXPH1	7.3
DCN	11.8	L3MBTL4	10.1	LINGO2	8.5	BC038556	7.3
FAM111B	11.6	THC2682885	9.9	IGFN1	8.5	CYB5A	7.3
DLGAP1	11.6	A_32_P226525	9.9	ARPP21	8.5	MGAT4C	7.3
SEMA3A	11.5	FABP3	9.8	MMRN1	8.5	BASP1	7.2
STAU2	11.5	CRISP1	9.8	BX538139	8.5	THC2700145	7.2
ABCB4	11.4	VAV1	9.7	GALNT4	8.5	FBN2	7.2
A_32_P172716	11.3	SOX9	9.7	IRX5	8.4	CASP10	7.2
SLC8A1	11.2	DDX60L	9.7	FOXA1	8.2	ODZ3	7.2
LMO3	11.2	SEMA6A	9.6	ENO3	8.2	MSX2P1	7.2
CRB1	11.1	DUSP27	9.6	MYH11	8.2	C20orf160	7.1
OCLN	11.0	DDX60	9.5	THC2520542	8.2	RHOH	7.1
WDR72	11.0	GPR162	9.5	DTX3L	8.2	EPHA10	7.1
KLHDC9	11.0	ASXL3	9.5	TRIM53P	8.1	THC2744399	7.1
DLC1	10.9	A1CF	9.4	NTS	8.1	KCTD16	7.0
CDH18	10.9	THC2677011	9.4	A_32_P4318	8.1	CARTPT	7.0
MLH1	10.9	LUM	9.3	PARP9	8.1	LOC100506674	7.0
ALPK2	10.9	TRIM34	9.3	KCNS1	8.1	DCLK1	7.0
ARID5B	10.7	ETV7	9.2	TMEM74	8.0	POC1B	7.0
MAT1A	10.7	ARPP21	9.2	SUSD1	8.0	P2RY6	7.0
MYL10	10.7	BEX1	9.2	CP	8.0	HSBP1L1	6.9
HOXB8	10.6	NDNF	9.2	MET	8.0	HOXD8	6.9
FRMD7	10.6	FIGN	9.2	SP140	7.9	MEST	6.9
GBP1	10.5	ZNF585A	9.2	TYRP1	7.9	CASP10	6.9
ENST00000504916	10.5	AQP9	9.1	GNB5	7.9	HEY1	6.8
C5	10.5	VAMP8	9.1	A_32_P225328	7.9	A1CF	6.8
GRIN3A	10.5	ADM	9.1	COL6A3	7.8	A_24_P489649	6.8
CXADR	10.5	ARID5B	9.1	A_24_P919283	7.8	BC031250	6.8
ASB2	10.5	PSMB9	9.0	ERV9-1	7.7	SP100	6.7
MSX2	10.5	OCLN	9.0	A_32_P100379	7.7	ABCA3	6.7
XAF1	10.4	SYT1	9.0	ESRRG	7.6	PACSIN1	6.7
GBP1	10.4	FILIP1	9.0	TMPRSS15	7.6	RTKN2	6.6
GRM8	10.3	LOC100288911	8.9	KIF1A	7.5	IGFLR1	6.6

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ENST00000531488	6.6	LZTS1	5.8	HOXB6	5.3	DNMT3B	4.8
MYL7	6.5	BBOX1	5.8	SGCE	5.2	A_23_P314024	4.7
BAALC	6.5	GBP3	5.7	RBM43	5.2	CD69	4.7
DGKB	6.5	QRFPR	5.7	THC2636875	5.2	RIMS2	4.7
SLC5A12	6.5	VIL1	5.7	FES	5.2	DHRS2	4.7
VGLL3	6.4	CXADR	5.7	ACTL8	5.2	ADAMTS3	4.7
PUS7L	6.3	ARG2	5.7	PLA2G3	5.2	TMCC3	4.7
NRP1	6.3	LOC100131733	5.7	MT1X	5.1	MT2A	4.6
ENKUR	6.3	IRF9	5.7	LPAR3	5.1	CCNB3	4.6
TNNT2	6.3	PHF20	5.7	FOXA1	5.1	METTL7A	4.6
A_32_P106980	6.3	HOXB6	5.7	ODZ3	5.1	MATN2	4.6
OCLN	6.3	IFITM1	5.7	CNDP1	5.1	NLGN1	4.6
MT1X	6.2	IFI30	5.6	NTRK3	5.1	WFIKKN1	4.6
D4S234E	6.2	XAF1	5.6	HRASLS2	5.1	SMCR5	4.6
CAV1	6.2	PLA2G3	5.6	FUT1	5.0	FBLN2	4.6
KITLG	6.2	HSBP1L1	5.6	MT2A	5.0	VCAN	4.6
BUB3	6.2	MAB21L2	5.6	PAIP2B	5.0	KANK1	4.6
AK027541	6.1	JPH2	5.6	IL26	5.0	SEMA3A	4.6
AK021664	6.1	VMO1	5.6	THC2524341	5.0	GSTT2	4.6
ITGA2	6.1	DYNC1I1	5.5	LXN	5.0	ARRDC4	4.6
KHDC1	6.1	FRY	5.5	TRIM15	5.0	ADAMTS1	4.6
ENST00000456585	6.1	CXCR7	5.5	CU675788	4.9	MYEF2	4.5
THC2642537	6.1	CXCR4	5.5	ENST00000519753	4.9	SIX1	4.5
RTKN2	6.1	TPD52L1	5.5	APOL1	4.9	CD19	4.5
THC2676635	6.1	CORO2A	5.5	SP140L	4.9	MT1H	4.5
A_32_P154321	6.1	C3orf58	5.5	SLITRK1	4.9	ATP2B1	4.5
ENST00000415106	6.1	PSMB8	5.4	PPP1R3B	4.9	DUSP6	4.5
NGEF	6.0	UBE2L6	5.4	ZNF506	4.9	FIGN	4.5
VAV3	6.0	MT2A	5.4	INPP5D	4.9	AMOT	4.5
PYGM	6.0	C21orf56	5.4	ENST00000421735	4.9	CKMT1A	4.5
FIBIN	6.0	XIRP2	5.4	ERC2	4.9	USP18	4.5
FAR2	6.0	P2RX5	5.4	LOC151174	4.8	NLRC5	4.5
BX092137	5.9	GSTT2	5.4	CAV2	4.8	KCNJ2	4.5
SORT1	5.9	ACTN3	5.4	MT1L	4.8	DNAH7	4.5
DBNDD2	5.9	A_24_P686243	5.3	GALNT4	4.8	CT45A1	4.5
LOC375295	5.9	HOXB9	5.3	SOX2	4.8	TRPV2	4.5
BTNL9	5.9	MT1E	5.3	GAD1	4.8	PSMB10	4.4
CEND1	5.9	NMI	5.3	TAP1	4.8	RCAN1	4.4
LOC440040	5.8	CA14	5.3	CA2	4.8	NTF4	4.4
AF086154	5.8	RNF144B	5.3	A_32_P194704	4.8	RAB3IP	4.4
ANXA10	5.8	CBLN2	5.3	FAM183B	4.8	LINC00478	4.4

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
LIX1	4.4	DUSP23	4.1	THC2654127	3.8	ENST00000485364	3.6
CAPS2	4.4	ZFPM2	4.1	ZP3	3.8	HOXB7	3.6
PLEKHA2	4.4	PML	4.1	C5orf39	3.8	A_32_P207789	3.6
BM552308	4.3	CEP44	4.1	CGREF1	3.8	APOBEC3C	3.5
LTB	4.3	ADAMTS1	4.1	PASK	3.8	MANSC1	3.5
AF074982	4.3	THC2704911	4.1	MITF	3.8	HLA-A	3.5
HEYL	4.3	HLA-B	4.0	HLA-H	3.8	MT1B	3.5
SNTG1	4.3	C16orf74	4.0	CKMT1A	3.8	BUB1	3.5
MPPED2	4.3	RAB3D	4.0	B3GALT1	3.8	HES1	3.5
IDO1	4.3	ERBB4	4.0	MGST2	3.8	MEG3	3.5
FAM133A	4.3	AF034187	4.0	DKFZP564C152	3.8	RTKN2	3.5
FAM164C	4.3	THC2603239	4.0	HLA-C	3.8	DOCK10	3.5
PRKAR1B	4.3	LAYN	4.0	TAS1R1	3.8	PCDHB8	3.5
DMKN	4.2	POU3F2	4.0	MT1H	3.7	A_24_P673119	3.5
THC2648509	4.2	LOC100240734	4.0	PNMAL1	3.7	HIST1H4B	3.5
A_23_P125109	4.2	THC2539492	4.0	FLT3LG	3.7	THC2537856	3.5
USP18	4.2	AK022035	3.9	LGALS3BP	3.7	LOC100507186	3.5
TRIB2	4.2	KIAA0182	3.9	HLA-B	3.7	FOLR1	3.5
PTX3	4.2	PIH1D2	3.9	LDHD	3.7	BMPER	3.5
MAOA	4.2	RAB3D	3.9	GRRP1	3.7	RANBP17	3.5
SLC2A4	4.2	OTOA	3.9	PAX9	3.7	SIX4	3.5
MT1G	4.2	DHRS2	3.9	SCLY	3.7	ENST00000557691	3.5
LOC644662	4.2	HOXD3	3.9	UCP2	3.7	SIK2	3.5
ASB1	4.2	HTATIP2	3.9	METTL7B	3.7	ALDH4A1	3.5
LOXL1	4.2	C16orf86	3.9	SLC2A1	3.7	HCP5	3.5
LOX	4.2	FZD5	3.9	A_32_P14737	3.7	C8orf4	3.5
AA455656	4.2	SHISA3	3.9	A_24_P7750	3.7	ASRGL1	3.5
LOC375295	4.1	LOC283174	3.9	ERAP2	3.6	ABHD8	3.5
C2orf77	4.1	RARRES3	3.9	PVRL2	3.6	A_24_P101771	3.5
TRIM64	4.1	MLLT3	3.9	FRZB	3.6	PML	3.5
FBXO16	4.1	PDZRN4	3.9	LRP1B	3.6	SLITRK6	3.5
RBM47	4.1	PCDH7	3.9	THC2697412	3.6	HIST1H4L	3.5
TFPI2	4.1	SPOCK2	3.9	VPS13A	3.6	FLJ36000	3.5
AK092921	4.1	NUP210	3.8	BX648207	3.6	IL20RB	3.5
ST8SIA1	4.1	ATP1A2	3.8	HIST1H4C	3.6	ARHGAP4	3.5
CYP26A1	4.1	ASRGL1	3.8	TRIM49	3.6	C9orf100	3.5
PDZD2	4.1	FAM182B	3.8	HDAC4	3.6	CDX2	3.5
PARP14	4.1	AK054718	3.8	KLF5	3.6	ETV1	3.5
C8orf51	4.1	GBP5	3.8	MCCC2	3.6	HLA-G	3.5
CAMK4	4.1	NR6A1	3.8	TMEM37	3.6	MST4	3.4
BC043357	4.1	SLC48A1	3.8	ENST00000432751	3.6	IRF1	3.4

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SH3BP4	3.4	HLA-J	3.2	KLRC1	3.1	BNIP3	3.0
NAV3	3.4	DTX3L	3.2	HOXD1	3.1	C10orf125	3.0
TOM1L2	3.4	MSH3	3.2	HLA-E	3.1	HIST1H1B	3.0
OR10A4	3.4	ENST00000375673	3.2	HLA-E	3.1	TIMP3	2.9
GLDC	3.4	BF737038	3.2	APOL6	3.1	CASP4	2.9
ECHS1	3.4	EBI3	3.2	CSF2RA	3.1	CCR1	2.9
A_32_P155588	3.4	SIGIRR	3.2	VPS13A	3.1	COMTD1	2.9
PML	3.4	ANXA9	3.2	APOBEC3F	3.1	HIST1H2AB	2.9
PARP14	3.4	BM458245	3.2	KIAA0182	3.1	FAM59A	2.9
RAB26	3.4	METTL12	3.2	VPS13A	3.1	CU687617	2.9
PLAC1	3.4	THC2496215	3.2	CXADR	3.1	ZFP36L1	2.9
CHCHD10	3.4	ANK1	3.2	NFIA	3.1	TRIM6	2.9
FAM183A	3.4	RIMKLA	3.2	TMEM92	3.1	MLF1	2.9
MYLK	3.4	TFEC	3.2	TRERF1	3.1	PBX3	2.9
THC2730631	3.4	HIST1H4D	3.2	A_32_P100206	3.1	THC2675966	2.9
CDT1	3.4	THC2713242	3.2	LOC100240735	3.0	DTYMK	2.9
ENST00000375678	3.4	AK124778	3.2	ALDH6A1	3.0	HLA-C	2.9
IFIT3	3.4	ZNF507	3.2	ZIC4	3.0	HLA-C	2.9
KIAA0101	3.3	ABCA1	3.2	C10orf125	3.0	H2AFJ	2.9
COBLL1	3.3	SPC24	3.2	HLA-A	3.0	TRIM6	2.9
PPM1F	3.3	HLA-H	3.2	AK125351	3.0	FH	2.9
FARP2	3.3	LOC100506268	3.2	PLK1	3.0	NUDT16L1	2.9
NUP210	3.3	TNNT2	3.2	H19	3.0	RDH10	2.9
SUCNR1	3.3	GAD1	3.2	HLA-F	3.0	AL049990	2.9
CCR10	3.3	PEG10	3.2	FOXP2	3.0	REC8	2.9
LOC100287177	3.3	A_32_P75141	3.2	TNNT2	3.0	PODXL	2.9
MGST1	3.3	ALDH1A2	3.2	OGDH	3.0	KCNMA1	2.9
FBXO15	3.3	HLA-C	3.1	MLF1	3.0	LAMA1	2.9
A_32_P99804	3.3	STAT1	3.1	SFRP1	3.0	OAS3	2.9
BU685399	3.3	M84605	3.1	ABCC6	3.0	FAM5C	2.9
TBC1D12	3.3	LOC100505683	3.1	PML	3.0	A_24_P418744	2.9
ST3GAL5	3.3	LBX1	3.1	PACSIN1	3.0	RASSF7	2.9
ANK1	3.3	COPS8	3.1	FZD5	3.0	BC038432	2.9
ZDHHC12	3.3	AK095167	3.1	PNKD	3.0	ARMC9	2.9
CARHSP1	3.3	HLA-B	3.1	ETV1	3.0	CNTNAP2	2.9
BX110727	3.3	HLA-B	3.1	CNIH3	3.0	PRPH2	2.9
LOC100652730	3.3	MAPK12	3.1	GCAT	3.0	DDT	2.9
ESPNL	3.3	CFD	3.1	AY143171	3.0	LOC100507487	2.9
THC2707492	3.3	KIAA1671	3.1	DTYMK	3.0	TMEM160	2.9
FBXL5	3.2	THC2787314	3.1	ENST00000539135	3.0	CRABP2	2.9
SLC27A5	3.2	IL32	3.1	GCA	3.0	WNK2	2.9

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
FOXO4	2.9	RASSF7	2.7	COTL1	2.7	FW340012	2.6
LOC100240735	2.9	STX18	2.7	FZD5	2.7	USP41	2.6
MITF	2.9	GK	2.7	GDF11	2.7	PHF15	2.6
NEXN-AS1	2.8	BC012528	2.7	TMEM100	2.7	ANXA11	2.6
BTN3A3	2.8	DNAH7	2.7	UPP1	2.7	CASZ1	2.6
THC2740030	2.8	ANO7	2.7	HLA-A	2.7	PPP2R1B	2.6
ENC1	2.8	MFI2	2.7	SMPD3	2.7	AK095300	2.6
D2HGDH	2.8	OSR2	2.7	GUK1	2.7	PSME2	2.6
ARID5B	2.8	CU686711	2.7	AV647560	2.7	PHF15	2.6
PECR	2.8	HMMR	2.7	ZDHHC2	2.6	E2F2	2.6
RHOU	2.8	MYBPH	2.7	TRIM69	2.6	SLC25A41	2.6
FAM195A	2.8	ZNF439	2.7	A_32_P760762	2.6	CFH	2.6
MUC4	2.8	CPPED1	2.7	LOC100505938	2.6	MTERFD2	2.6
DHRS3	2.8	CLGN	2.7	HSPB2	2.6	KANK2	2.6
TTC13	2.8	KLHDC10	2.7	FLOT2	2.6	STX18	2.6
GBP4	2.8	GAD1	2.7	SORCS1	2.6	GFER	2.6
CAMK1D	2.8	HLA-E	2.7	WDR63	2.6	A_32_P121978	2.6
NXNL2	2.8	PARD6A	2.7	DAND5	2.6	TMEM63A	2.6
THC2682560	2.8	NUDT16L1	2.7	FOXN4	2.6	ASF1B	2.6
ZDHHC24	2.8	LOC100289361	2.7	AA158952	2.6	MYEOV2	2.6
A_32_P183987	2.8	CDC42EP3	2.7	A_23_P133949	2.6	SLC25A10	2.6
HBQ1	2.8	CARD6	2.7	CHRNA9	2.6	ZIC4	2.6
AGBL2	2.8	C1QTNF6	2.7	CASP4	2.6	PRCP	2.6
E2F7	2.8	DLGAP5	2.7	AK074144	2.6	CASP5	2.6
NLRC5	2.8	DDC	2.7	ZDHHC2	2.6	FAM133A	2.6
ADH1C	2.8	OBFC2A	2.7	A_32_P51313	2.6	FANCI	2.6
HES1	2.8	ASRGL1	2.7	THC2582300	2.6	HSD17B6	2.6
STK33	2.8	LOC729887	2.7	NP111779	2.6	HAAO	2.6
MYLK	2.8	KIAA1217	2.7	AFMID	2.6	AK024956	2.6
BEND4	2.8	GMPPB	2.7	RDH10	2.6	IARS2	2.6
ATP6V0D2	2.8	BTN3A2	2.7	AFAP1L1	2.6	DBP	2.5
IQCD	2.8	ISYNA1	2.7	DONSON	2.6	GRIK5	2.5
RIC3	2.7	PAIP2B	2.7	COTL1	2.6	ITGAM	2.5
TMEM106C	2.7	CDCA2	2.7	LRTOMT	2.6	NTPCR	2.5
GPR126	2.7	ING5	2.7	C2CD4C	2.6	AGPAT4	2.5
DDX58	2.7	SUV420H2	2.7	LPAR3	2.6	BI832578	2.5
RPL22L1	2.7	CGN	2.7	THC2770932	2.6	EXO1	2.5
ACTG2	2.7	AKR1B1	2.7	ICA1	2.6	HIP1	2.5
LRBA	2.7	A_32_P42213	2.7	LOC439911	2.6	AB062488	2.5
ADAMTS3	2.7	A_24_P938006	2.7	HSD17B11	2.6	CDT1	2.5
HIVEP3	2.7	COTL1	2.7	ZMYM5	2.6	SNX5	2.5

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
CCDC116	2.5	UBE2H	2.4	PRKD2	2.4	DFNB31	2.3
SNAI1	2.5	FAM59A	2.4	HIST1H2BD	2.4	SLC2A4RG	2.3
GSTM3	2.5	CU690251	2.4	POLR2L	2.4	BSPRY	2.3
CTAG1A	2.5	VPS13A	2.4	LYRM5	2.4	SOX1	2.3
EPHA5	2.5	HIST1H1D	2.4	RABL5	2.4	A_32_P187160	2.3
KIAA0564	2.5	CCNG1	2.4	CDH12	2.4	ProSAPiP1	2.3
BST2	2.5	MACF1	2.4	VEGFB	2.4	SLC48A1	2.3
KRT222	2.5	MED11	2.4	NUAK2	2.4	ACAT1	2.3
APOL6	2.5	C1orf85	2.4	GATS	2.4	C19orf46	2.3
C16orf55	2.5	DEPDC4	2.4	RHOBTB1	2.4	DENND5B	2.3
B2M	2.5	SOCS3	2.4	CDC45	2.4	BAIAP2L2	2.3
WDR34	2.5	FGF21	2.4	CABIN1	2.4	GPC3	2.3
BC032755	2.5	CEP70	2.4	AK058115	2.4	BCAT2	2.3
KBTBD3	2.5	PIH1D1	2.4	ARMC9	2.4	LGI3	2.3
VPS13A	2.5	A_32_P5628	2.4	AIF1L	2.4	TRIM24	2.3
TPM1	2.5	THAP4	2.4	RARG	2.4	BROX	2.3
DDB2	2.5	POLD3	2.4	JMJD7	2.4	CCNA2	2.3
GRB14	2.5	NDUFA10	2.4	CTSK	2.4	FBXO27	2.3
ATPBD4	2.5	ARID3A	2.4	ARAP1	2.4	RNF187	2.3
MTMR9LP	2.5	VAMP5	2.4	RFC5	2.4	GLI3	2.3
RIMKLA	2.5	DQX1	2.4	SARDH	2.4	C11orf83	2.3
NUDT1	2.5	H3F3A	2.4	LOC100506268	2.4	AL566369	2.3
TNNI3	2.5	DHRS11	2.4	STRADB	2.4	GMIP	2.3
ZIC1	2.5	C8orf85	2.4	MYLPF	2.4	ENST00000551107	2.3
A_24_P144134	2.5	PPIP5K1	2.4	THC2499508	2.4	BC037328	2.3
AK092681	2.5	JUP	2.4	MOP-1	2.4	METTL21A	2.3
RHOU	2.5	GUK1	2.4	RILP	2.4	CABIN1	2.3
ESCO2	2.5	THC2526765	2.4	NTHL1	2.4	PTTG2	2.3
TPD52	2.5	TBXA2R	2.4	HIST1H4J	2.4	MRPL55	2.3
THC2675062	2.5	SCAND1	2.4	WNT10B	2.4	PPP2R1B	2.3
THC2535223	2.5	TMEM69	2.4	BC018626	2.4	A_32_P15169	2.3
THC2689623	2.5	DONSON	2.4	VASN	2.3	C18orf56	2.3
A_24_P230288	2.5	DAB2IP	2.4	ANXA11	2.3	IKBKE	2.3
C6orf226	2.5	PSME1	2.4	LTK	2.3	PKN3	2.3
FAM122C	2.5	SIGLEC11	2.4	CLDND2	2.3	CCDC134	2.3
FAIM	2.5	VEGFC	2.4	TRIM22	2.3	TSPAN4	2.3
OCEL1	2.5	A_23_P251196	2.4	CNIH4	2.3	ASTL	2.3
PRKAR1B	2.5	FANCI	2.4	DEGS1	2.3	DOCK3	2.3
FRMD4A	2.5	RGS3	2.4	SYNGR1	2.3	A_24_P560431	2.3
CDKN2A	2.5	RFC3	2.4	ORMDL2	2.3	AIM1L	2.3
CORO2A	2.5	A_24_P7040	2.4	PCSK7	2.3	KCNJ4	2.3

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
FAM188B	2.3	ZNF695	2.2	PIGQ	2.2	THC2538534	2.2
UQCR10	2.3	IFITM3	2.2	GAMT	2.2	HSD17B11	2.2
HMGCLL1	2.3	CHODL	2.2	RALGAPA2	2.2	BORA	2.2
ENST00000430027	2.3	RILP	2.2	TIGD2	2.2	DHFR	2.2
MYBL2	2.3	A_23_P392897	2.2	PBK	2.2	CARD17	2.2
TIMMDC1	2.3	THC2757602	2.2	BPNT1	2.2	C9orf150	2.2
THC2656479	2.3	CHAF1B	2.2	A_32_P21742	2.2	PRKACB	2.2
PRIM1	2.3	SCAI	2.2	NDUFA10	2.2	COX5B	2.2
SCHIP1	2.3	METTL21A	2.2	RNPEPL1	2.2	APOM	2.2
AV707615	2.3	AA019203	2.2	RFX5	2.2	KIAA1671	2.2
TFPI	2.3	NEXN	2.2	SNRNP25	2.2	LOC100505932	2.2
BTN3A2	2.3	RHOF	2.2	CTH	2.2	SNHG13	2.2
ZFP106	2.3	CCNB1	2.2	TLN2	2.2	PRKAA1	2.2
APRT	2.3	ATP5D	2.2	TK1	2.2	PRKAR1B	2.2
PRR5-ARHGAP8	2.3	OSBPL9	2.2	RGNEF	2.2	CR622072	2.2
TSPAN4	2.3	MDM1	2.2	TAGLN	2.2	MRPL28	2.2
DIAPH2	2.3	MSH3	2.2	A_24_P332953	2.2	BC010544	2.2
NDUFAF3	2.3	OXCT1	2.2	PLS1	2.2	OIP5	2.2
NUDT22	2.3	SHMT1	2.2	WDR24	2.2	ADNP2	2.1
TAF8	2.3	ENAH	2.2	DICER1-AS	2.2	C9orf23	2.1
CDH9	2.3	CENPI	2.2	AF090930	2.2	SLC25A23	2.1
A_32_P65157	2.3	KIF1C	2.2	FZR1	2.2	C16orf59	2.1
STK25	2.3	HSDL2	2.2	DLAT	2.2	WDHD1	2.1
HPS3	2.3	A_24_P323682	2.2	COMMD4	2.2	PPP1R35	2.1
SLC39A4	2.3	NDUFB10	2.2	TCOF1	2.2	PXMP4	2.1
A_24_P600603	2.2	BM129308	2.2	NDUFB1	2.2	MELK	2.1
L1CAM	2.2	THC2575678	2.2	ALAD	2.2	ZFHX2	2.1
ABCA7	2.2	TMUB1	2.2	WWOX	2.2	C12orf62	2.1
NUSAP1	2.2	TPD52	2.2	THC2648791	2.2	SLC38A5	2.1
AK128413	2.2	THRA	2.2	PSRC1	2.2	TXNIP	2.1
HIVEP2	2.2	ACTA2	2.2	METTL11A	2.2	TRIM5	2.1
TEC	2.2	TDRD7	2.2	TNNC1	2.2	ING5	2.1
POLR2L	2.2	A_24_P944478	2.2	MTERFD2	2.2	RBM41	2.1
IQCE	2.2	CECR2	2.2	CAMKMT	2.2	CHML	2.1
OBSCN	2.2	STRBP	2.2	CBX5	2.2	C7orf50	2.1
RPH3AL	2.2	MUC1	2.2	SCLY	2.2	DEPDC1	2.1
THC2762599	2.2	EHBP1L1	2.2	AB593167	2.2	LOC400043	2.1
LINC00346	2.2	TDRD1	2.2	A_23_P72014	2.2	BX537510	2.1
ACCN2	2.2	SLC25A4	2.2	F11R	2.2	EMG1	2.1
THC2746571	2.2	A_23_P142197	2.2	GATS	2.2	OSR2	2.1
RAD54B	2.2	KYNU	2.2	SLC30A1	2.2	H3F3A	2.1

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
BU853136	2.1	STK17B	2.1	BI836406	2.1	SPC25	2.0
CRYBB2P1	2.1	CCDC24	2.1	TAGLN	2.1	COMMD4	2.0
ALDH4A1	2.1	SKP2	2.1	TSPAN6	2.1	CISD3	2.0
DLAT	2.1	DEPDC1	2.1	DHRS13	2.1	CLDN17	2.0
PPP1R9A	2.1	STK25	2.1	NDUFB3	2.1	ARL2	2.0
HDLBP	2.1	DPM3	2.1	NR1H3	2.1	CENPI	2.0
A_32_P118896	2.1	MLF1	2.1	CENPF	2.1	AA554330	2.0
GPSM3	2.1	DPM3	2.1	STAC2	2.1	NUCKS1	2.0
IFI35	2.1	CCDC34	2.1	TUSC2	2.1	ACYP1	2.0
PPPDE1	2.1	ZIC1	2.1	HIST1H2AG	2.1	SLC30A9	2.0
GPN2	2.1	INSIG2	2.1	HDLBP	2.1	NANOG	2.0
ENST00000494075	2.1	NVL	2.1	ZNF580	2.1	MDM1	2.0
NUCKS1	2.1	AIF1L	2.1	LOC100507303	2.1	LRRC70	2.0
LOC100288798	2.1	SCO2	2.1	FBXW9	2.1	CXXC5	2.0
ENST00000432961	2.1	MT1G	2.1	NDUFS8	2.1	RARG	2.0
CCDC50	2.1	BCAS4	2.1	HCFC1R1	2.1	NPM1	2.0
LMNB1	2.1	ALDH4A1	2.1	THC2748857	2.1	HIST1H3A	2.0
WDR62	2.1	LOC100507475	2.1	EPHX1	2.1	CU689917	2.0
CTSE	2.1	GRHL3	2.1	SLC43A2	2.1	PIDD	2.0
H2AFJ	2.1	CDH10	2.1	SEC61A2	2.1	ITGA6	2.0
P2RX5	2.1	PCDH17	2.1	AURKB	2.1	ALKBH7	2.0
MRPL55	2.1	SCD5	2.1	SEMA6B	2.1	ANGPTL4	2.0
RASGEF1A	2.1	A_24_P178167	2.1	PLIN5	2.1	POLD1	2.0
ENST00000428471	2.1	RASIP1	2.1	ENST00000517816	2.0	LOC100130557	2.0
PTBP2	2.1	SLX1A	2.1	MCM3AP-AS1	2.0	RASSF4	2.0
TMEM52	2.1	APBB2	2.1	ATG4B	2.0	C20orf96	2.0
HIST1H4K	2.1	TBL1X	2.1	RMI2	2.0	FNBP1	2.0
A_32_P159289	2.1	HOXB3	2.1	TJP2	2.0	NCAPH	2.0
BBS5	2.1	G2E3	2.1	CDC20	2.0	BC141946	2.0
GMNN	2.1	LOC100506190	2.1	PPP1R7	2.0	RGS9BP	2.0
IFITM3	2.1	H3F3A	2.1	HIST2H4B	2.0	SPAG5	2.0
MMS22L	2.1	CEP70	2.1	POP7	2.0	NR1D1	2.0
CDCA3	2.1	HIST1H4F	2.1	STAU2	2.0	FBXO3	2.0
MAPRE1	2.1	RNASEH2A	2.1	CCDC28B	2.0	HIST1H4I	2.0
HPS3	2.1	ECT2	2.1	NUDT21	2.0	NUP133	2.0
RNF26	2.1	PTTG1	2.1	AK054756	2.0	B9D1	2.0
GTPBP5	2.1	NAT6	2.1	MEF2BNB	2.0	ISG15	2.0
TMEM93	2.1	CRYBB2	2.1	C1orf172	2.0	OBSCN	2.0
SLC25A23	2.1	REEP6	2.1	FGD6	2.0	NACC2	2.0
KIF20A	2.1	AIG1	2.1	SLC25A23	2.0	ACN9	2.0
MRPL41	2.1	ENST00000356370	2.1	IFT81	2.0	STAT1	2.0

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
C22orf39	2.0	AK127081	-2.0	M14087	-2.0	ERLIN1	-2.0
BCKDK	2.0	A_24_P915634	-2.0	MCTS1	-2.0	A_24_P499481	-2.0
BG612665	2.0	A_32_P62137	-2.0	H3F3B	-2.0	C17orf101	-2.0
UGCG	2.0	A_24_P93052	-2.0	ZFHX3	-2.0	ADRA2C	-2.0
HMGB2	2.0	ASAP3	-2.0	SLC3A2	-2.0	SKI	-2.0
ARAP1	2.0	CLK2	-2.0	TXLNA	-2.0	METTL21A	-2.0
SIVA1	2.0	ZNF396	-2.0	MAP4K5	-2.0	MYO6	-2.0
TRAPPC2L	2.0	PCGF3	-2.0	TRIM4	-2.0	TMEM35	-2.0
SLC30A1	2.0	EEPD1	-2.0	AK055647	-2.0	LOC100133331	-2.0
KIF1C	2.0	ARHGEF19	-2.0	A_32_P60632	-2.0	A_24_P118382	-2.0
CCNB2	2.0	SRSF1	-2.0	CCDC57	-2.0	TH1L	-2.0
HIST2H2AC	2.0	CSTF2T	-2.0	GUSBP11	-2.0	AF088004	-2.0
ISOC1	2.0	PTPN14	-2.0	THC2541781	-2.0	A_24_P290214	-2.0
POLR2L	2.0	A_24_P900721	-2.0	CR749547	-2.0	DCAF4	-2.0
ZNF107	2.0	AK054806	-2.0	AK056855	-2.0	TNFRSF12A	-2.0
PITX1	2.0	FBXO11	-2.0	FAM92A3	-2.0	HLA-DRB5	-2.0
CHEK1	2.0	GOLGA6L9	-2.0	PDCD11	-2.0	SLC30A6	-2.0
POLD1	2.0	EIF5	-2.0	ACTR5	-2.0	AL390214	-2.0
NAT14	2.0	TYSND1	-2.0	B4GALNT1	-2.0	HIST1H3B	-2.0
SHPK	2.0	CEP95	-2.0	IPO7	-2.0	A_24_P488510	-2.0
APEH	2.0	C18orf55	-2.0	DEPDC7	-2.0	CHMP7	-2.0
FKBP11	2.0	ADAT1	-2.0	PPIE	-2.0	DBIL5P	-2.0
KANK2	2.0	RNMT	-2.0	MED10	-2.0	A_24_P739582	-2.0
SHF	-2.0	SHC1	-2.0	NPIPL2	-2.0	NFIB	-2.0
DSTYK	-2.0	VCP	-2.0	ADCY1	-2.0	ENST00000538228	-2.0
LHFPL4	-2.0	UBXN2A	-2.0	AY033611	-2.0	UFD1L	-2.0
ZNRF1	-2.0	TNRC6C	-2.0	TUBB4A	-2.0	SHPRH	-2.0
SLC39A13	-2.0	FTL	-2.0	GHITM	-2.0	LAMP2	-2.0
A_24_P152345	-2.0	SPARC	-2.0	THC2737176	-2.0	THC2694186	-2.0
ZNF516	-2.0	SNX13	-2.0	C14orf79	-2.0	GOLGA2P2Y	-2.0
RAP1GAP2	-2.0	HEXA	-2.0	DUSP16	-2.0	ZCRB1	-2.0
NUDT4	-2.0	DYNLT1	-2.0	FUCA1	-2.0	AM181370	-2.0
DNAJC30	-2.0	LRP1	-2.0	A_24_P853366	-2.0	LOC399744	-2.0
NSFL1C	-2.0	A_24_P565503	-2.0	STK40	-2.0	EG327585	-2.0
ENST00000399269	-2.0	A_24_P332780	-2.0	FAM91A1	-2.0	ARHGEF10	-2.0
IKZF5	-2.0	SSH2	-2.0	TAPT1	-2.0	SUV420H1	-2.0
LEAP2	-2.0	ADAM9	-2.0	LRRC41	-2.0	NS3BP	-2.0
EWSR1	-2.0	ZNF211	-2.0	SRSF7	-2.0	GOLGA6L9	-2.0
ATRN	-2.0	A_24_P350252	-2.0	SDCBP	-2.0	SYVN1	-2.0
ENST00000399576	-2.0	HOPX	-2.0	FRG1B	-2.0	ARMC9	-2.0
C17orf108	-2.0	CREBZF	-2.0	TUBB2A	-2.0	DKK3	-2.0

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
OXR1	-2.0	NBR1	-2.1	ZNF121	-2.1	MAPK8IP3	-2.1
UBE2Q2P1	-2.0	CNN3	-2.1	ATP4A	-2.1	OPN1LW	-2.1
AK097166	-2.0	CYTH2	-2.1	RBMS3	-2.1	ANKRD40	-2.1
FLJ45340	-2.0	FBXO10	-2.1	CB985069	-2.1	ZNF577	-2.1
ATAD2B	-2.0	DECR1	-2.1	SNPH	-2.1	PLEKHM3	-2.1
SPOP	-2.0	ELOVL3	-2.1	KLHDC5	-2.1	FAM101B	-2.1
UBL3	-2.0	A_24_P230388	-2.1	TROVE2	-2.1	CBWD5	-2.1
THC2528427	-2.0	CEP97	-2.1	PNMA5	-2.1	MICB	-2.1
DOCK9	-2.0	HDDC2	-2.1	THC2500237	-2.1	OTX1	-2.1
A_23_P124177	-2.0	MIB2	-2.1	LOC100507493	-2.1	AK022223	-2.1
PARP6	-2.0	ENST00000542270	-2.1	ENST00000555377	-2.1	HMBOX1	-2.1
TAPT1	-2.0	ZFP161	-2.1	AK026485	-2.1	NUDT4	-2.1
BCL2L11	-2.0	PGM2	-2.1	ZNF285	-2.1	CACNA1H	-2.1
PCOLCE2	-2.0	CYR61	-2.1	UBOX5	-2.1	KIDINS220	-2.1
PRRG1	-2.0	SEC63	-2.1	TRNP1	-2.1	KGFLP1	-2.1
PLDN	-2.0	PIGM	-2.1	ACRC	-2.1	C1orf9	-2.1
ICMT	-2.0	MCMBP	-2.1	TMEM101	-2.1	TAOK3	-2.1
SH3KBP1	-2.0	AB019568	-2.1	ZSCAN18	-2.1	ERLEC1	-2.1
MAPKAP1	-2.0	A_32_P9931	-2.1	PTAR1	-2.1	SPRED1	-2.1
C6orf203	-2.0	A_23_P130187	-2.1	ATAD1	-2.1	CRADD	-2.1
FNIP2	-2.0	C3orf23	-2.1	PCDHB7	-2.1	ENST00000448494	-2.1
USP3	-2.0	WIPF2	-2.1	CMTM6	-2.1	THC2648397	-2.1
CRYM	-2.0	A_24_P234871	-2.1	AF143882	-2.1	A_24_P152855	-2.1
A_32_P205139	-2.0	C6orf228	-2.1	A_32_P190097	-2.1	A_24_P33403	-2.1
ACADVL	-2.0	DHCR24	-2.1	CYBRD1	-2.1	CHCHD7	-2.1
ENST00000537149	-2.0	NUDT4	-2.1	STMN3	-2.1	A_24_P516728	-2.1
PAQR9	-2.0	ERCC4	-2.1	TMEFF1	-2.1	PLEKHA3	-2.1
PDCD2	-2.0	ENST00000434399	-2.1	CRYL1	-2.1	RHOQ	-2.1
ZNF2	-2.0	TAC1	-2.1	MBOAT2	-2.1	ELF1	-2.1
MAP3K10	-2.0	MGAT5	-2.1	PODXL2	-2.1	SNX18	-2.1
ZBED1	-2.0	A_32_P15898	-2.1	MORN4	-2.1	RASD1	-2.1
SNX13	-2.0	OXCT2	-2.1	CPT1A	-2.1	IKZF5	-2.1
C2orf18	-2.0	SLC38A4	-2.1	DCAF10	-2.1	A_24_P837537	-2.1
A_24_P834066	-2.0	A_32_P213948	-2.1	RBMS3	-2.1	SOCS6	-2.1
SPRYD7	-2.0	RUFY2	-2.1	AF116616	-2.1	TRAF3	-2.1
RAPGEF1	-2.0	VPS54	-2.1	NCOR1	-2.1	TRUB1	-2.1
PRAME	-2.1	CEBPA	-2.1	CLK1	-2.1	UBL3	-2.1
A_24_P135579	-2.1	MPHOSPH10	-2.1	OR12D3	-2.1	CEBPA	-2.1
C6orf48	-2.1	A_24_P126731	-2.1	DNAH10	-2.1	C7orf13	-2.1
EDEM3	-2.1	ZCCHC2	-2.1	ANKRD18A	-2.1	CCDC84	-2.1
FNBP1L	-2.1	ENST00000415212	-2.1	A_24_P289504	-2.1	NEK1	-2.1

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
PDXDC2P	-2.1	TLK2	-2.1	A_24_P502752	-2.1	TPM4	-2.1
C20orf3	-2.1	TAF12	-2.1	PHF14	-2.1	BC014023	-2.1
TPM4	-2.1	THC2570021	-2.1	BIRC2	-2.1	PDCD6IP	-2.1
MEGF9	-2.1	TMEM104	-2.1	DNAJC27	-2.1	TRAF3	-2.1
A_24_P616082	-2.1	VCP	-2.1	BRD4	-2.1	ZNF507	-2.1
RBM8A	-2.1	APLP2	-2.1	NR1D2	-2.1	ACYP2	-2.1
BCL2L11	-2.1	ANXA2P3	-2.1	TPM4	-2.1	TMEM201	-2.1
SPAG9	-2.1	P4HA2	-2.1	BG534208	-2.1	DPH3	-2.1
HGF	-2.1	ZNF234	-2.1	AKIRIN2-AS1	-2.1	RBM8A	-2.1
CN294989	-2.1	A_24_P705136	-2.1	C6orf164	-2.1	AK024389	-2.1
CRK	-2.1	C14orf79	-2.1	KAZN	-2.1	TRA2B	-2.1
GLT25D2	-2.1	MICB	-2.1	MCTS1	-2.1	BC035247	-2.1
ZNF419	-2.1	MYH3	-2.1	A_32_P13081	-2.1	SNX17	-2.1
DKK1	-2.1	ZNF420	-2.1	RBAK	-2.1	CPT1A	-2.1
GNAQ	-2.1	GOLGA3	-2.1	HSPA13	-2.1	ANKRD11	-2.1
A_32_P139909	-2.1	UBE2J1	-2.1	A_32_P132883	-2.1	A_24_P452175	-2.1
EPDR1	-2.1	BC003519	-2.1	ZNF283	-2.1	ENDOD1	-2.1
CCDC91	-2.1	SNRK	-2.1	BCL10	-2.1	A_24_P24453	-2.1
MYH9	-2.1	SEPT7P2	-2.1	A_24_P32715	-2.1	USP11	-2.1
PLAGL1	-2.1	AK095453	-2.1	IGFBP4	-2.1	LUC7L3	-2.1
AK022183	-2.1	RAB22A	-2.1	C17orf74	-2.1	LPP	-2.1
DMD	-2.1	SAP18	-2.1	PRKAR1A	-2.1	C20orf177	-2.1
A_32_P46112	-2.1	GAS5	-2.1	FAM21C	-2.1	CTSC	-2.1
UGGT2	-2.1	FGFR1	-2.1	SEC63	-2.1	FAM43B	-2.1
EML4	-2.1	MAP1A	-2.1	SERINC1	-2.1	MTRF1L	-2.1
A_23_P17152	-2.1	DCLRE1C	-2.1	ITPRIP	-2.1	FBXO11	-2.1
ANKRD20A9P	-2.1	PLP2	-2.1	CD63	-2.1	ARF4	-2.1
SAT1	-2.1	NBPF10	-2.1	DHFRL1	-2.1	THC2586905	-2.1
PDGFD	-2.1	GCOM1	-2.1	A_24_P118813	-2.1	CAHM	-2.1
ENST00000480427	-2.1	SASH1	-2.1	RNASEL	-2.1	PI15	-2.1
RBMX	-2.1	PSMD12	-2.1	FAM120C	-2.1	SEMA4F	-2.1
TM9SF2	-2.1	THC2615379	-2.1	A_24_P835388	-2.1	POGLUT1	-2.1
THC2493376	-2.1	THC2662279	-2.1	ITPKC	-2.1	CASP7	-2.1
TP73-AS1	-2.1	CDC37L1	-2.1	SLC26A11	-2.1	SLC35A1	-2.1
CDON	-2.1	HIST1H3C	-2.1	C9orf3	-2.1	ITM2B	-2.1
PARP4	-2.1	MST1	-2.1	GATC	-2.1	MAPK8	-2.1
APPL2	-2.1	AK027225	-2.1	CD59	-2.1	PRKAR1A	-2.1
STAG3	-2.1	GDF15	-2.1	SLC39A11	-2.1	PVRL1	-2.1
LOC100128164	-2.1	TM9SF3	-2.1	C6orf35	-2.1	A_32_P16451	-2.1
HIST2H3D	-2.1	UPRT	-2.1	AK307360	-2.1	IMPAD1	-2.1
DCAF4	-2.1	LOC100506710	-2.1	XPNPEP1	-2.1	UBE2J2	-2.1

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SAMD4B	-2.1	MFAP2	-2.2	A_24_P502660	-2.2	BC034930	-2.2
DCAF7	-2.1	A_24_P229903	-2.2	A_32_P124727	-2.2	ACYP2	-2.2
ENST00000370708	-2.1	MGAT4B	-2.2	UAP1L1	-2.2	TNFRSF25	-2.2
TPRKB	-2.1	AA176161	-2.2	FBXW4P1	-2.2	C6orf204	-2.2
C6orf64	-2.1	HSPA5	-2.2	GPR157	-2.2	ENST00000425338	-2.2
CCNJ	-2.1	UCN	-2.2	STX4	-2.2	ANKRD50	-2.2
NDFIP2	-2.1	SNX29	-2.2	ENST00000419235	-2.2	USP6	-2.2
ISM2	-2.1	PLOD2	-2.2	ZNF711	-2.2	A_24_P84719	-2.2
KIAA1549	-2.1	ZNF354A	-2.2	SS18L1	-2.2	SOS2	-2.2
ZFP36L2	-2.1	ZNF529	-2.2	ZNF493	-2.2	AF271776	-2.2
RSU1	-2.1	C9orf41	-2.2	FLJ14186	-2.2	THC2674068	-2.2
OFD1	-2.1	NBPF3	-2.2	TCF25	-2.2	THC2525188	-2.2
ISL2	-2.1	ANKRD43	-2.2	APBA2	-2.2	C10orf46	-2.2
ZFP90	-2.1	UBE2D1	-2.2	PCMTD2	-2.2	PKDCC	-2.2
NDUFC2	-2.1	PQLC2	-2.2	HIST2H2AA4	-2.2	EFCAB1	-2.2
STT3B	-2.1	RUNDC3A	-2.2	SAR1A	-2.2	RNF112	-2.2
BRF2	-2.1	PIAS4	-2.2	TRIM44	-2.2	SGPL1	-2.2
GLTSCR1	-2.2	PTCH1	-2.2	FOXO3	-2.2	SLC16A5	-2.2
ZNF732	-2.2	TMEM87A	-2.2	MTHFD1L	-2.2	ACAD11	-2.2
A_24_P930487	-2.2	COL16A1	-2.2	IFIT2	-2.2	MXI1	-2.2
EP300	-2.2	FAM126A	-2.2	NMU	-2.2	LOC100506571	-2.2
NOVA1	-2.2	DDX3Y	-2.2	AGAP2	-2.2	A_24_P273074	-2.2
ZNF696	-2.2	EEF1A1	-2.2	KIAA0090	-2.2	BLOC1S2	-2.2
ITPKC	-2.2	ADAM22	-2.2	ZRANB1	-2.2	MRPS23	-2.2
GPR180	-2.2	FRA10AC1	-2.2	STEAP1	-2.2	DYRK2	-2.2
DND1	-2.2	LIG4	-2.2	C9orf30	-2.2	VSIG10	-2.2
AMT	-2.2	CRY2	-2.2	NOC2L	-2.2	CX783461	-2.2
LAPTM4A	-2.2	ENST00000512848	-2.2	A_32_P193952	-2.2	THC2727164	-2.2
A_24_P780319	-2.2	LZIC	-2.2	C21orf2	-2.2	SOBP	-2.2
ZNF114	-2.2	TMEM64	-2.2	GPR172B	-2.2	PAPSS2	-2.2
A_24_P118391	-2.2	UBQLN1	-2.2	HDAC5	-2.2	CASP2	-2.2
RHOB	-2.2	CERS5	-2.2	FGD3	-2.2	SOCS5	-2.2
EXOC7	-2.2	AADAT	-2.2	TPRG1L	-2.2	DPYSL2	-2.2
GOLGA6L9	-2.2	MAN2C1	-2.2	MBNL2	-2.2	ADAMTS2	-2.2
ANKRD20A2	-2.2	PALM2-AKAP2	-2.2	MBOAT2	-2.2	ZNF227	-2.2
AK124192	-2.2	SEC31B	-2.2	TEX19	-2.2	KIF1B	-2.2
CCDC76	-2.2	LPP	-2.2	HABP4	-2.2	LOC100507265	-2.2
CCDC104	-2.2	RNF166	-2.2	MICAL2	-2.2	LARP6	-2.2
ZRANB1	-2.2	SYT11	-2.2	EMP3	-2.2	MED23	-2.2
TMEM120B	-2.2	CDV3	-2.2	PPM1F	-2.2	AA631975	-2.2
CEBPE	-2.2	ENST00000390252	-2.2	LYRM7	-2.2	A_24_P409410	-2.2

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
FAM92A1	-2.2	MZT2A	-2.2	C5orf25	-2.2	ATP10A	-2.3
IBTK	-2.2	AF116641	-2.2	A_24_P221475	-2.2	UFM1	-2.3
SLC30A7	-2.2	RDH14	-2.2	A_32_P183656	-2.2	FAM190B	-2.3
ITPR3	-2.2	EXOC7	-2.2	A_24_P458252	-2.2	FGGY	-2.3
MCOLN2	-2.2	AK4	-2.2	B4GALT5	-2.2	A_24_P636974	-2.3
SLC1A3	-2.2	ZNF638	-2.2	TET2	-2.2	A_24_P118719	-2.3
THC2701140	-2.2	LINGO1	-2.2	FIBCD1	-2.2	HERC4	-2.3
A_24_P852099	-2.2	CLCN3	-2.2	A_23_P78975	-2.2	CDC40	-2.3
NT5C3L	-2.2	FAM120B	-2.2	ZNF513	-2.2	STXBP6	-2.3
AARSD1	-2.2	ZC3H7B	-2.2	BM678681	-2.2	FOSB	-2.3
FDFT1	-2.2	TOM1L2	-2.2	ME1	-2.2	C15orf2	-2.3
PLXNA1	-2.2	CAPZA2	-2.2	A_24_P839075	-2.2	AA630774	-2.3
CEACAM21	-2.2	KIAA1875	-2.2	TRIM7	-2.2	LOC100505573	-2.3
ZFAND5	-2.2	PTRF	-2.2	H3F3B	-2.2	B4GALNT1	-2.3
HNRNPA1P27	-2.2	FAM106A	-2.2	FOXK2	-2.2	SPRED1	-2.3
BC013295	-2.2	PYGO1	-2.2	TRAK2	-2.2	C16orf79	-2.3
DNPEP	-2.2	POTEG	-2.2	WDFY2	-2.2	ARRDC2	-2.3
EIF2AK3	-2.2	BC063381	-2.2	A_24_P306614	-2.2	MLXIPL	-2.3
PTPRJ	-2.2	RGS1	-2.2	EFHB	-2.2	TRIO	-2.3
ZNF473	-2.2	KLHDC5	-2.2	PGS1	-2.2	CALCOCO2	-2.3
A_24_P489639	-2.2	CYP51A1	-2.2	A_24_P24786	-2.2	RUFY3	-2.3
ZNF519	-2.2	AGRP	-2.2	SOCS5	-2.2	OSTM1	-2.3
M27126	-2.2	HADHA	-2.2	ZNF329	-2.2	AK055716	-2.3
A_24_P577289	-2.2	CEBPD	-2.2	IQSEC1	-2.2	PPAP2B	-2.3
AK092508	-2.2	CLK2	-2.2	SRP19	-2.2	PTRF	-2.3
A_24_P786713	-2.2	DDIT4	-2.2	GRIA4	-2.2	THC2691966	-2.3
TRIM41	-2.2	DCAF7	-2.2	MAGED2	-2.2	E2F6	-2.3
METTL3	-2.2	LOC202181	-2.2	LOC729732	-2.2	RAB13	-2.3
SYTL1	-2.2	A_24_P670342	-2.2	C17orf99	-2.2	RIOK1	-2.3
THC2560357	-2.2	FSTL1	-2.2	BC030138	-2.2	SMURF2	-2.3
CYP2D6	-2.2	GOLGA6L10	-2.2	SLK	-2.2	RHO	-2.3
ZNF697	-2.2	LRP5L	-2.2	E2F6	-2.2	KIAA0930	-2.3
CCDC47	-2.2	ATF5	-2.2	AK054852	-2.2	C2orf42	-2.3
ADAM9	-2.2	BX476711	-2.2	TMEM22	-2.2	FAM21C	-2.3
JMJD6	-2.2	UBTF	-2.2	A_23_P60189	-2.2	ENGASE	-2.3
HDAC9	-2.2	SLC39A10	-2.2	ZNF283	-2.3	CYP51A1	-2.3
C19orf28	-2.2	SREBF2	-2.2	A_24_P58242	-2.3	TMEM194A	-2.3
ZNF248	-2.2	ENST00000413722	-2.2	E2F6	-2.3	TMEM17	-2.3
ZBTB49	-2.2	AA666384	-2.2	ENST00000532936	-2.3	C11orf54	-2.3
THC2635591	-2.2	PPP3R1	-2.2	ZNRF1	-2.3	ENST00000447310	-2.3
A_24_P464798	-2.2	ZNF295	-2.2	TESK1	-2.3	THC2543840	-2.3

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
PPME1	-2.3	RSAD1	-2.3	YBX2	-2.3	SCD	-2.3
DLG2	-2.3	A_24_P461497	-2.3	MEX3B	-2.3	UNKL	-2.3
PURA	-2.3	FBXO25	-2.3	GRK5	-2.3	EDEM1	-2.3
ALPK1	-2.3	RPL32P3	-2.3	B4GALT5	-2.3	NBPF11	-2.3
A_32_P174374	-2.3	TSC22D1	-2.3	THC2704037	-2.3	ZNF367	-2.3
EIF3F	-2.3	LHPP	-2.3	THC2643296	-2.3	LOC100132790	-2.3
UTRN	-2.3	ZNF225	-2.3	IGLL1	-2.3	THC2598564	-2.3
PCMT1	-2.3	ENST00000521369	-2.3	XBP1	-2.3	RIOK3	-2.3
GOLGA6L9	-2.3	GOLGA2	-2.3	ENST00000360902	-2.3	MOB1B	-2.3
FAM174A	-2.3	H3F3C	-2.3	ADARB1	-2.3	KIAA1919	-2.3
MANEAL	-2.3	GPAM	-2.3	USP27X	-2.3	MYO9A	-2.3
THC2512545	-2.3	HM358951	-2.3	PHLDA1	-2.3	TWIST1	-2.3
PAPOLG	-2.3	ENST00000553155	-2.3	E2F6	-2.3	MSRA	-2.3
CTAGE5	-2.3	GSN	-2.3	PDCD2	-2.3	ZNF259P1	-2.3
IL27RA	-2.3	ZNF77	-2.3	STRN	-2.3	THBS1	-2.3
NAALAD2	-2.3	THC2650352	-2.3	FAM165B	-2.3	BY796363	-2.3
FXYD6	-2.3	HSPA5	-2.3	LOC554207	-2.3	CASK	-2.3
SLC16A2	-2.3	CK430712	-2.3	A_24_P571937	-2.3	FAM171B	-2.3
SNAI2	-2.3	SIRPG	-2.3	ZNF181	-2.3	NACAP1	-2.3
THC2577186	-2.3	A_24_P451992	-2.3	ARHGAP23	-2.3	ZMAT1	-2.3
ZNF252	-2.3	NPC2	-2.3	TRIB1	-2.3	CSAG1	-2.3
NFXL1	-2.3	PAQR6	-2.3	ATP10D	-2.3	DDX50	-2.3
CU690321	-2.3	RNF185	-2.3	BSDC1	-2.3	DNAJB2	-2.3
A_32_P128399	-2.3	ENST00000447898	-2.3	C10orf32	-2.3	PCDHB2	-2.3
HIPK3	-2.3	INPP4B	-2.3	KRT10	-2.3	FGFR1	-2.3
GOLT1B	-2.3	NUPL1	-2.3	GAA	-2.3	HAB1	-2.3
BBS5	-2.3	CCDC82	-2.3	SEMA4F	-2.3	ITGB5	-2.3
WWC2	-2.3	CACNG8	-2.3	BAIAP2	-2.3	A_23_P144317	-2.3
PLA2G12A	-2.3	ARL8A	-2.3	PDP2	-2.3	HSD17B7	-2.3
NEBL	-2.3	ATP7A	-2.3	NAGK	-2.3	ZDHHC6	-2.3
POM121L8P	-2.3	A_24_P263803	-2.3	SGPP1	-2.3	IDI2-AS1	-2.3
THC2563307	-2.3	SETD5	-2.3	TSPYL4	-2.3	RNF141	-2.3
PDCD6IP	-2.3	EPB41L4B	-2.3	DENND4A	-2.3	ENDOD1	-2.3
GPRASP1	-2.3	SMPDL3A	-2.3	LOC389033	-2.3	MASP2	-2.3
C16orf52	-2.3	ENST00000399576	-2.3	KLF13	-2.3	A_24_P937424	-2.3
A_24_P289477	-2.3	KLHL17	-2.3	C9orf93	-2.3	KLF11	-2.3
COPG2	-2.3	TP73	-2.3	NELL2	-2.3	TSPAN14	-2.3
AKR1C1	-2.3	HADHA	-2.3	LOC100190939	-2.3	CAPN12	-2.3
CCNL2	-2.3	AK057167	-2.3	LYG1	-2.3	MOSPD2	-2.3
PPME1	-2.3	MYO1G	-2.3	RGS2	-2.3	A_24_P565496	-2.3
FASN	-2.3	ROCK2	-2.3	C9orf72	-2.3	LOC338620	-2.3

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
MTMR4	-2.3	USP32P2	-2.4	TTTY5	-2.4	ZDHHC22	-2.4
A_24_P213396	-2.3	DDX10	-2.4	LOC100132790	-2.4	TBRG1	-2.4
DNAJB2	-2.3	MBTPS1	-2.4	STON1	-2.4	ACBD7	-2.4
PDE4DIP	-2.3	MTHFD1L	-2.4	A_24_P255763	-2.4	SMAP2	-2.4
H6PD	-2.3	NECAP1	-2.4	SECISBP2L	-2.4	PCMTD2	-2.4
FGB	-2.3	LCOR	-2.4	A_32_P11701	-2.4	KDSR	-2.4
TTC17	-2.3	VEZF1	-2.4	OGT	-2.4	A_24_P106166	-2.4
REL	-2.3	FAM172A	-2.4	MGC70870	-2.4	ATP6V0A1	-2.4
SLC6A13	-2.3	TBC1D16	-2.4	AK022848	-2.4	PHLDA2	-2.4
DNM3OS	-2.3	POTEM	-2.4	ARHGEF15	-2.4	MINPP1	-2.4
LOC100287525	-2.3	BZW1	-2.4	MTMR9	-2.4	DOCK11	-2.4
A_24_P914922	-2.3	BTN2A1	-2.4	PCDH10	-2.4	A_24_P350017	-2.4
MADCAM1	-2.3	A_24_P375573	-2.4	WTAP	-2.4	RHOQ	-2.4
POGLUT1	-2.3	ACAP3	-2.4	WWTR1	-2.4	PPFIBP1	-2.4
KCNV2	-2.3	SPATA20	-2.4	ACSL1	-2.4	MYO1C	-2.4
ANK2	-2.3	POLB	-2.4	JAM3	-2.4	THC2656699	-2.4
CYP2B6	-2.3	TMEM194A	-2.4	CYB5R1	-2.4	SAP30L	-2.4
WNT10A	-2.3	KIF7	-2.4	A_24_P229766	-2.4	CEP112	-2.4
MALAT1	-2.3	SPACA3	-2.4	AL521247	-2.4	PINK1	-2.4
EAF1	-2.3	TMEM51	-2.4	ZNF850	-2.4	THC2659814	-2.4
LOC100133920	-2.3	UNK	-2.4	NOTCH2NL	-2.4	ZNF558	-2.4
DISP1	-2.3	ROCK1	-2.4	A_32_P73707	-2.4	NPHP4	-2.4
TUBE1	-2.3	CDC40	-2.4	SOSTDC1	-2.4	CSRNP2	-2.4
MTRF1L	-2.3	THC2594845	-2.4	ITPRIPL2	-2.4	PLEKHA1	-2.4
THC2565422	-2.3	CDH15	-2.4	SPPL2A	-2.4	CAPRIN2	-2.4
CEBPB	-2.3	PFKFB2	-2.4	MXRA7	-2.4	MST1P2	-2.4
DLK2	-2.3	MOSPD1	-2.4	NBPF15	-2.4	A_32_P184039	-2.4
SNX29	-2.4	MMP16	-2.4	JRKL	-2.4	LOC100131581	-2.4
GSTM2P1	-2.4	LOC100287590	-2.4	TECPR2	-2.4	NCOA1	-2.4
FER1L4	-2.4	CPT1B	-2.4	KLHL3	-2.4	ENST00000428709	-2.4
TMEM65	-2.4	FRMD8	-2.4	SCD	-2.4	FAS	-2.4
A_23_P47220	-2.4	VEZF1	-2.4	HGF	-2.4	NDN	-2.4
GPR135	-2.4	EHD3	-2.4	NBPF10	-2.4	FOXA3	-2.4
KIAA1656	-2.4	A_24_P230100	-2.4	RCAN3	-2.4	DCAKD	-2.4
SOCS6	-2.4	LOC643837	-2.4	FAM134C	-2.4	NPEPPS	-2.4
STEAP1	-2.4	MFGE8	-2.4	A_32_P93792	-2.4	BX111592	-2.4
PGM5	-2.4	ZNF236	-2.4	CASD1	-2.4	DECR1	-2.4
ARVCF	-2.4	KCNN4	-2.4	A_32_P155043	-2.4	JUNB	-2.4
ZNF583	-2.4	A_23_P115902	-2.4	TRIB3	-2.4	AZI2	-2.4
TPM4	-2.4	NMUR1	-2.4	ENST00000449958	-2.4	TM9SF3	-2.4
WDR43	-2.4	TSNARE1	-2.4	MED29	-2.4	ACTB	-2.4

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
CCT5	-2.4	BC018676	-2.4	MAP3K5	-2.5	C15orf17	-2.5
LRRC39	-2.4	ZNF813	-2.4	AGAP8	-2.5	OXNAD1	-2.5
APPBP2	-2.4	C6orf62	-2.4	PCDHA1	-2.5	A_24_P307184	-2.5
A_24_P530977	-2.4	OTUD3	-2.4	PHF20L1	-2.5	AKAP11	-2.5
CLTC	-2.4	PRKAR1A	-2.4	CEP63	-2.5	C3orf20	-2.5
ANKRD36BP2	-2.4	PDZD8	-2.4	ROCK1P1	-2.5	PLEKHA4	-2.5
MRC2	-2.4	ZNF26	-2.4	BI497361	-2.5	THC2496620	-2.5
AK123264	-2.4	PHF20L1	-2.5	THC2693923	-2.5	STMN3	-2.5
AGAP8	-2.4	NMNAT1	-2.5	GRAMD4	-2.5	A_24_P289130	-2.5
PRKCA	-2.4	C10orf2	-2.5	LOC100292680	-2.5	ZNF596	-2.5
PBLD	-2.4	CB529149	-2.5	MGEA5	-2.5	PLA2G4F	-2.5
WTAP	-2.4	A_24_P230466	-2.5	BC014023	-2.5	SPTY2D1	-2.5
AW972815	-2.4	ENST00000416851	-2.5	THC2644335	-2.5	ENST00000537659	-2.5
AKNA	-2.4	ENDOV	-2.5	A_24_P502652	-2.5	A_24_P281468	-2.5
A_32_P125736	-2.4	RET	-2.5	CRTC3	-2.5	BRD2	-2.5
DYNC2LI1	-2.4	ZNF273	-2.5	GOLGA4	-2.5	GJA1	-2.5
BOD1L	-2.4	A_24_P560332	-2.5	SNX29	-2.5	LAMC3	-2.5
TMEM47	-2.4	NPLOC4	-2.5	COL13A1	-2.5	A_24_P682550	-2.5
AK090397	-2.4	STRN	-2.5	FAM107B	-2.5	THC2654993	-2.5
NRL	-2.4	CPA4	-2.5	A_32_P49164	-2.5	ENST00000390622	-2.5
ITSN2	-2.4	A_24_P92267	-2.5	OSCAR	-2.5	FBN1	-2.5
THC2533833	-2.4	C10orf88	-2.5	TMIE	-2.5	RRP15	-2.5
GOLGA1	-2.4	BQ272125	-2.5	KIF1B	-2.5	MMP1	-2.5
BE184907	-2.4	THC2520478	-2.5	C10orf32	-2.5	C6orf225	-2.5
NBPF9	-2.4	KRCC1	-2.5	C2orf27A	-2.5	ROCK2	-2.5
ZNF160	-2.4	FAM184A	-2.5	AHI1	-2.5	KIAA2018	-2.5
ATP8B2	-2.4	A_24_P585660	-2.5	AGAP7	-2.5	A_24_P641673	-2.5
FCGRT	-2.4	ENST00000531225	-2.5	IL23A	-2.5	MICA	-2.5
RALGDS	-2.4	PANK2	-2.5	NFE2L1	-2.5	ICA1L	-2.5
OTUB2	-2.4	PSAP	-2.5	A_23_P206568	-2.5	THC2539273	-2.5
AI698357	-2.4	PHIP	-2.5	IDUA	-2.5	PPAPDC2	-2.5
ZNF850	-2.4	AF075008	-2.5	CTAGE7P	-2.5	ACYP2	-2.5
TBC1D30	-2.4	USP27X	-2.5	WTAP	-2.5	KIAA1462	-2.5
RHBDF1	-2.4	IBTK	-2.5	PRSS23	-2.5	SNAI2	-2.5
AF010144	-2.4	ABAT	-2.5	MTDH	-2.5	SLC35E1	-2.5
YIPF4	-2.4	OSGIN1	-2.5	SCARNA17	-2.5	FAM120B	-2.5
TAOK3	-2.4	CBX6	-2.5	PIGH	-2.5	CEP112	-2.5
A_32_P47616	-2.4	RIPK2	-2.5	LOC100499177	-2.5	NBPF14	-2.5
A_32_P28158	-2.4	A_24_P58759	-2.5	A_24_P871726	-2.5	AL833005	-2.5
USP32	-2.4	THC2717828	-2.5	A_24_P508946	-2.5	TRIM23	-2.5
A_23_P72252	-2.4	HIPK3	-2.5	UBE2G2	-2.5	A_24_P383901	-2.5

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ZNF154	-2.5	GMCL1	-2.5	RAPGEF6	-2.6	PDXDC2P	-2.6
SETX	-2.5	SLC45A3	-2.5	GALNTL4	-2.6	LIF	-2.6
LOC100507486	-2.5	AK125099	-2.5	FGFRL1	-2.6	LOC100129794	-2.6
AV753543	-2.5	NADK	-2.5	ENST00000471093	-2.6	HPS1	-2.6
ZFAND2A	-2.5	ALAS1	-2.5	AL049390	-2.6	PP7080	-2.6
THC2669419	-2.5	NETO2	-2.5	SARM1	-2.6	A_32_P24295	-2.6
HSD17B14	-2.5	USP32P1	-2.5	CN430296	-2.6	PCMT1	-2.6
CDK20	-2.5	CALCOCO2	-2.5	RHCG	-2.6	CD518596	-2.6
PXN	-2.5	OAT	-2.5	CCDC82	-2.6	CCL3	-2.6
THC2643084	-2.5	MEX3A	-2.5	CTTN	-2.6	THC2624360	-2.6
A_24_P869138	-2.5	HECTD2	-2.5	BUB3	-2.6	ENST00000519648	-2.6
NP414419	-2.5	MFSD2A	-2.5	AK023559	-2.6	LOC100130691	-2.6
USP42	-2.5	CCNT1	-2.5	IFRD1	-2.6	AK091034	-2.6
THC2736130	-2.5	ENST00000445515	-2.5	ZNF284	-2.6	PPME1	-2.6
SNX13	-2.5	PDXDC2P	-2.5	KPNA5	-2.6	LDLRAD3	-2.6
KLHDC5	-2.5	MRPL43	-2.5	BC010266	-2.6	KIAA1549	-2.6
DOPEY1	-2.5	CCDC159	-2.5	FAM21C	-2.6	CAST	-2.6
MEX3A	-2.5	DKK3	-2.5	WIF1	-2.6	A_24_P366465	-2.6
DNM3OS	-2.5	FAM21C	-2.5	NEFL	-2.6	GOPC	-2.6
MICU1	-2.5	LEMD3	-2.5	HEBP2	-2.6	LOC100288144	-2.6
KIAA0930	-2.5	MRAP2	-2.5	THC2731042	-2.6	ARMCX3	-2.6
DUSP3	-2.5	EPB41L4B	-2.5	PREPL	-2.6	LRRC8C	-2.6
TMEM64	-2.5	BC014971	-2.5	THC2536014	-2.6	POTEE	-2.6
CDKN1C	-2.5	USP36	-2.5	SOLH	-2.6	LOC653075	-2.6
PVR	-2.5	PPP1CB	-2.5	LOC728739	-2.6	DNAJC12	-2.6
LOC647979	-2.5	IDI1	-2.5	RET	-2.6	FOXO3	-2.6
A_24_P780353	-2.5	A_24_P298099	-2.5	DCAF16	-2.6	COL6A2	-2.6
RAD17	-2.5	PARP11	-2.6	A_32_P147297	-2.6	PGCP	-2.6
KCNG1	-2.5	PSTK	-2.6	CCDC57	-2.6	MEIS1	-2.6
NETO2	-2.5	ZNF25	-2.6	LOC84989	-2.6	SPTBN1	-2.6
BC033227	-2.5	BBIP1	-2.6	TWIST2	-2.6	PLD1	-2.6
ZNF423	-2.5	THC2673973	-2.6	RPS6KA6	-2.6	C20orf194	-2.6
BLOC1S2	-2.5	C6orf192	-2.6	LRRC47	-2.6	AK023412	-2.6
CBWD6	-2.5	FPGS	-2.6	C6orf89	-2.6	A_24_P33385	-2.6
LOC100133161	-2.5	MTHFR	-2.6	FOXC1	-2.6	ME1	-2.6
LOC100129033	-2.5	A_24_P247175	-2.6	FOS	-2.6	PPFIBP1	-2.6
FAM92A1	-2.5	PKD2	-2.6	KCNH3	-2.6	LRP11	-2.6
NT5DC3	-2.5	ARHGAP27	-2.6	NID1	-2.6	STX4	-2.6
TMEM41B	-2.5	ENST00000504184	-2.6	POTEF	-2.6	RNF13	-2.6
KCNMA1	-2.5	HEATR6	-2.6	NBPF11	-2.6	FAM120AOS	-2.6
THC2572360	-2.5	BEND3	-2.6	FGFBP3	-2.6	PABPC3	-2.6

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
PCDHA11	-2.6	RIC8B	-2.6	IFIT5	-2.7	RTN4	-2.7
THC2631150	-2.6	LOC100133161	-2.6	RAB11FIP2	-2.7	ZFAND5	-2.7
A_24_P631948	-2.6	PHACTR2	-2.6	A_24_P144337	-2.7	ENST00000421003	-2.7
THC2524424	-2.6	CLIP1	-2.6	SOCS7	-2.7	LINC00265	-2.7
THC2645336	-2.6	NCOA7	-2.6	ZCCHC18	-2.7	LOC100507780	-2.7
FBLN7	-2.6	RGS5	-2.6	ENST00000413768	-2.7	CHST3	-2.7
SOCS7	-2.6	KLC1	-2.6	CK823339	-2.7	C12orf66	-2.7
KBTBD8	-2.6	THC2678309	-2.6	A_32_P20717	-2.7	MAFG	-2.7
PLEKHA4	-2.6	LONRF1	-2.6	SMA4	-2.7	ACTC1	-2.7
BTG1	-2.6	ACSS2	-2.6	SEC24C	-2.7	STEAP1	-2.7
KAT6B	-2.6	TRIM54	-2.6	SNX16	-2.7	NDUFAF4	-2.7
GABPB2	-2.6	WWTR1	-2.6	ACBD5	-2.7	RAB11FIP2	-2.7
HRASLS5	-2.6	HCN3	-2.6	RPS6KB1	-2.7	AK123066	-2.7
PLGLB1	-2.6	RALGDS	-2.6	MXRA7	-2.7	LOC729088	-2.7
ROCK1	-2.6	A_24_P714620	-2.6	LOC84989	-2.7	TCP1	-2.7
FTH1	-2.6	CACNA1B	-2.7	AMOTL1	-2.7	CNKSR3	-2.7
LOC339524	-2.6	A_24_P475115	-2.7	AF237700	-2.7	BX097783	-2.7
MEX3B	-2.6	SUFU	-2.7	POM121	-2.7	SRXN1	-2.7
SAMD8	-2.6	C3orf51	-2.7	MYO6	-2.7	CTAGE5	-2.7
AZI2	-2.6	IL27RA	-2.7	UFL1	-2.7	THC2662244	-2.7
THC2712372	-2.6	ENST00000439904	-2.7	PHF2	-2.7	ANKRD23	-2.7
AL833005	-2.6	W22487	-2.7	A_32_P217581	-2.7	ICK	-2.7
C19orf6	-2.6	ADARB1	-2.7	POTEKP	-2.7	LOC80054	-2.7
REPS2	-2.6	AF075112	-2.7	MID1	-2.7	SERPINB9	-2.7
SNX29	-2.6	EIF5A2	-2.7	EPT1	-2.7	A_24_P144314	-2.7
AK091178	-2.6	NFIB	-2.7	THC2677630	-2.7	GRIK1	-2.7
A_24_P695669	-2.6	FZD1	-2.7	THC2667666	-2.7	THC2748290	-2.7
THC2666547	-2.6	TFE3	-2.7	A_24_P152974	-2.7	EHBP1	-2.7
BM455175	-2.6	NPM2	-2.7	AGAP7	-2.7	FTSJD1	-2.7
LOC441124	-2.6	PBLD	-2.7	MUM1L1	-2.7	GOLGA8IP	-2.7
BE780682	-2.6	RAP2B	-2.7	ZFAND5	-2.7	NOVA1	-2.7
NFKB2	-2.6	LRIG1	-2.7	BC000206	-2.7	LINC00341	-2.7
POU5F1	-2.6	A_32_P36481	-2.7	OBSL1	-2.7	PDXDC2P	-2.7
GREB1	-2.6	TTYH2	-2.7	AK057652	-2.7	COL24A1	-2.7
STX3	-2.6	C9orf125	-2.7	NEU1	-2.7	P4HA2	-2.7
PBX1	-2.6	GOLGA8F	-2.7	LOC221272	-2.7	SLC9A8	-2.7
A_24_P678056	-2.6	NFE2L1	-2.7	A_24_P611903	-2.7	EZR	-2.7
C14orf49	-2.6	MAP4K5	-2.7	OTUD3	-2.7	USP6	-2.7
GABPB2	-2.6	C10orf118	-2.7	WIF1	-2.7	LRRC1	-2.7
LOC643650	-2.6	ITGAV	-2.7	A_24_P83968	-2.7	DHRS7	-2.7
GGT7	-2.6	TNFRSF9	-2.7	THC2574606	-2.7	THC2503819	-2.7

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ADAMTS13	-2.7	TXNRD1	-2.8	TBC1D8B	-2.8	GTF2A1	-2.8
FLJ14186	-2.7	A_24_P7570	-2.8	THC2730719	-2.8	GOLGA6L9	-2.8
PNPLA8	-2.7	HEXIM1	-2.8	FTH1	-2.8	OXR1	-2.8
NBPF3	-2.7	HIST2H2AA4	-2.8	A_24_P161393	-2.8	AGAP7	-2.8
ENST00000390323	-2.7	KREMEN1	-2.8	FGF7	-2.8	PIP5K1A	-2.8
TET3	-2.7	AF126109	-2.8	LINC00338	-2.8	LOC648740	-2.8
BF575152	-2.7	BF217859	-2.8	TMEM185B	-2.8	UGGT2	-2.8
QKI	-2.7	ARHGAP32	-2.8	CLEC18B	-2.8	DUSP1	-2.8
SMYD3	-2.7	TP53AIP1	-2.8	HLA-DPA1	-2.8	SLC41A2	-2.8
A_24_P136155	-2.7	THC2726959	-2.8	AFTPH	-2.8	A_32_P131870	-2.8
ZNF140	-2.7	SGK3	-2.8	SLC35A1	-2.8	SLC22A23	-2.8
NIPBL	-2.7	ITPRIPL2	-2.8	STXBP6	-2.8	NFIL3	-2.8
THC2689802	-2.7	PDCD2	-2.8	HIF3A	-2.8	UBQLN4	-2.8
LGALSL	-2.7	MLXIPL	-2.8	NPIP	-2.8	GLA	-2.8
MSL3	-2.7	KLF10	-2.8	SPAG9	-2.8	GLCCI1	-2.8
BU567832	-2.7	IGLON5	-2.8	GORASP1	-2.8	LOC100170939	-2.8
MTHFR	-2.7	THC2741789	-2.8	LPP	-2.8	A_32_P22005	-2.8
PRX	-2.7	USP34	-2.8	THC2565608	-2.8	TTC37	-2.9
TTC7A	-2.7	GDAP1	-2.8	TMSB4X	-2.8	GOLGA8F	-2.9
NP113399	-2.7	BG695979	-2.8	BM683477	-2.8	CEP95	-2.9
A_32_P89480	-2.7	THC2713545	-2.8	SCD	-2.8	BX537816	-2.9
KIAA1211	-2.7	BC049371	-2.8	RHOQ	-2.8	LRP8	-2.9
PSMC5	-2.7	CEP290	-2.8	NFYA	-2.8	MUC5B	-2.9
OBFC1	-2.7	ARID1B	-2.8	SERTAD2	-2.8	TAC1	-2.9
NPPC	-2.7	AF187554	-2.8	SPATA13	-2.8	NRIP3	-2.9
SCPEP1	-2.7	ENST00000513644	-2.8	THC2653489	-2.8	THC2727102	-2.9
SP100	-2.7	C10orf35	-2.8	IFNGR1	-2.8	LRP8	-2.9
AK130366	-2.7	GPC2	-2.8	NR4A1	-2.8	MUC20	-2.9
AFTPH	-2.7	JMJD1C	-2.8	RAB32	-2.8	NAB2	-2.9
LONRF1	-2.7	RNF2	-2.8	AA968804	-2.8	NGLY1	-2.9
LOC100131564	-2.8	A_24_P264416	-2.8	CCDC126	-2.8	FAM149B1	-2.9
C1QL2	-2.8	FERMT1	-2.8	SYTL1	-2.8	HSPA14	-2.9
ELOVL4	-2.8	SHC1	-2.8	HLA-DPB1	-2.8	A_24_P660797	-2.9
C3orf64	-2.8	THC2706230	-2.8	A_24_P625683	-2.8	BACE1	-2.9
HIRA	-2.8	MMAB	-2.8	ZNF2	-2.8	A_24_P16361	-2.9
ANKRD20A2	-2.8	INE1	-2.8	A_32_P159023	-2.8	THC2749235	-2.9
METTL21A	-2.8	BC042589	-2.8	C14orf118	-2.8	A_23_P369758	-2.9
TNFRSF1A	-2.8	THC2620541	-2.8	A_24_P76210	-2.8	A_24_P255786	-2.9
TCP10	-2.8	LONRF1	-2.8	TMEM158	-2.8	BX101288	-2.9
SPACA4	-2.8	A_24_P174063	-2.8	CEP68	-2.8	PLEKHM1	-2.9
RAB11FIP4	-2.8	ENST00000330588	-2.8	DPYD	-2.8	CLCN6	-2.9

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
PCDHB2	-2.9	CA419971	-2.9	AK024602	-2.9	A_24_P324424	-3.0
AK000707	-2.9	C17orf58	-2.9	A_24_P49800	-3.0	LRRN2	-3.0
C19orf57	-2.9	ETS2	-2.9	MUCL1	-3.0	TOLLIP	-3.0
BAG3	-2.9	TRIOBP	-2.9	A_24_P187626	-3.0	MICAL1	-3.0
ASPHD2	-2.9	HEATR5B	-2.9	IFRD1	-3.0	AHI1	-3.0
EPS8	-2.9	ENST00000376445	-2.9	A_23_P216071	-3.0	MAP3K2	-3.0
PCYT1B	-2.9	NR4A2	-2.9	CR606969	-3.0	A_23_P119407	-3.0
DHCR24	-2.9	KIAA0889	-2.9	DTNB	-3.0	SRSF12	-3.0
HSD17B7	-2.9	PARVA	-2.9	RRP12	-3.0	FBXO25	-3.0
RAB24	-2.9	GNAZ	-2.9	RBMS3	-3.0	THC2679516	-3.0
LIPG	-2.9	NRG1	-2.9	SLC9B2	-3.0	THAP5	-3.0
THC2633081	-2.9	S81524	-2.9	SELS	-3.0	A_24_P332911	-3.0
RPS6KB1	-2.9	A_32_P27558	-2.9	ENST00000544461	-3.0	UBE2E1	-3.0
C3orf62	-2.9	P2RX1	-2.9	CCDC149	-3.0	CSGALNACT2	-3.0
TSC1	-2.9	A_24_P229728	-2.9	ASAP2	-3.0	METRNL	-3.0
AL137389	-2.9	AK054921	-2.9	ATMIN	-3.0	DENND2C	-3.0
SREBF2	-2.9	PCGF3	-2.9	PPFIBP1	-3.0	UCP3	-3.0
KLHL2	-2.9	A_24_P392947	-2.9	LOXL3	-3.0	AF086376	-3.0
SIX2	-2.9	A_32_P7193	-2.9	A_32_P190036	-3.0	TMEM8B	-3.0
FTH1	-2.9	CGNL1	-2.9	NUDT10	-3.0	RBMS3	-3.0
SMARCE1	-2.9	C9orf167	-2.9	MLH3	-3.0	SMAD9	-3.0
KCNJ14	-2.9	CD164	-2.9	C22orf43	-3.0	THC2692419	-3.0
NBPF1	-2.9	A_32_P169696	-2.9	MFGE8	-3.0	ARHGAP9	-3.0
THC2688475	-2.9	NP450512	-2.9	MLLT11	-3.0	A_24_P289043	-3.0
TTC15	-2.9	A_24_P929985	-2.9	SMAP2	-3.0	TMEM87B	-3.0
A_24_P647965	-2.9	ZNF471	-2.9	UBAP1L	-3.0	FAM160B1	-3.0
SLC30A6	-2.9	NPC1	-2.9	PLAA	-3.0	ZNF736	-3.0
A_32_P167212	-2.9	ENST00000421542	-2.9	ZNF251	-3.0	UBR4	-3.0
ZNF502	-2.9	MYBL1	-2.9	AKAP8L	-3.0	LOC100133091	-3.0
EIF5	-2.9	PURB	-2.9	MTNR1A	-3.0	CEP104	-3.0
ATP6V1G1	-2.9	A_24_P332721	-2.9	TTLL7	-3.0	AK124576	-3.0
SCAND3	-2.9	TMSB4X	-2.9	MLLT4	-3.0	KIAA1908	-3.0
REEP3	-2.9	KLHDC7B	-2.9	MPP3	-3.0	UBR3	-3.0
ENST00000448014	-2.9	MBD2	-2.9	IFNAR2	-3.0	ENST00000495461	-3.0
HIST2H2BE	-2.9	EPT1	-2.9	THC2507829	-3.0	AK024382	-3.0
GOLGA8A	-2.9	CTAGE10P	-2.9	BGN	-3.0	THC2717825	-3.0
TRIO	-2.9	C1orf226	-2.9	AK098220	-3.0	PDE4D	-3.0
PRKAB1	-2.9	MAP1LC3A	-2.9	GABRQ	-3.0	LOC100131289	-3.0
DMRTC1	-2.9	MPP3	-2.9	FNDC3B	-3.0	INPP5K	-3.0
SRSF8	-2.9	S100A3	-2.9	A_24_P401090	-3.0	SARS	-3.0
ENST00000423704	-2.9	C9orf125	-2.9	LOC100129387	-3.0	STXBP5	-3.0

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
CITED1	-3.0	CU678847	-3.1	BAIAP2	-3.1	AF010144	-3.2
THC2484716	-3.0	ZNF853	-3.1	ICAM4	-3.1	GCLM	-3.2
RGL3	-3.0	NEFL	-3.1	MFSD2A	-3.1	BX119882	-3.2
LOC643837	-3.0	GGT7	-3.1	GPR135	-3.1	ACAT2	-3.2
ANKRD20A2	-3.0	AK092875	-3.1	FTCD	-3.1	PPIL6	-3.2
A_24_P701814	-3.0	NANOS3	-3.1	FOSL2	-3.1	ENST00000424422	-3.2
IGDCC4	-3.0	RNASET2	-3.1	CHST2	-3.1	PAX4	-3.2
THC2636529	-3.0	COMMD6	-3.1	PRDM12	-3.1	IL17D	-3.2
ENST00000541329	-3.0	ITPRIPL2	-3.1	HERC2P7	-3.1	KLHL6	-3.2
THC2664391	-3.0	ITGB2	-3.1	HMGN5	-3.1	IL28RA	-3.2
LINC00265	-3.0	KAZALD1	-3.1	LOC729680	-3.1	POMC	-3.2
A_24_P144254	-3.0	JMJD1C	-3.1	SASH1	-3.1	TULP4	-3.2
ENST00000416851	-3.0	KDM6B	-3.1	A_24_P383199	-3.1	TMEM88	-3.2
Z69892	-3.0	MCF2L	-3.1	THAP5	-3.1	XKR4	-3.2
C8orf59	-3.1	ACTG1	-3.1	FAM172A	-3.1	AL832820	-3.2
THC2666687	-3.1	MAP3K2	-3.1	SRGAP1	-3.1	FLJ39653	-3.2
PVR	-3.1	TGFBR2	-3.1	LOC151009	-3.1	C10orf118	-3.2
THC2667190	-3.1	RRAGB	-3.1	NMNAT1	-3.1	SMAD9	-3.2
LRRK1	-3.1	MERTK	-3.1	CLCN3	-3.1	FOSL1	-3.2
GPRASP2	-3.1	ASAP2	-3.1	BET3L	-3.1	ZBTB40	-3.2
GPR161	-3.1	A_32_P172198	-3.1	NR4A3	-3.1	IGF2R	-3.2
DKFZP434K028	-3.1	ZBTB41	-3.1	A_32_P27964	-3.1	SH3BP5	-3.2
ZNF234	-3.1	LOXL2	-3.1	GPR161	-3.1	GPRC5C	-3.2
HGSNAT	-3.1	THC2556546	-3.1	AKAP12	-3.1	ZNF263	-3.2
MAFG	-3.1	MUC3A	-3.1	BE881987	-3.1	NUDT12	-3.2
MCC	-3.1	ENST00000443034	-3.1	RAB39B	-3.2	HIC1	-3.2
OSTM1	-3.1	LOC100506710	-3.1	TRIB3	-3.2	C6orf164	-3.2
RAPGEF2	-3.1	FKBP7	-3.1	AHNAK	-3.2	SMAGP	-3.2
DLX3	-3.1	DQ786266	-3.1	SLC22A5	-3.2	KCNIP3	-3.2
RSU1	-3.1	COX6B2	-3.1	PITPNM2	-3.2	STARD4	-3.2
THC2654921	-3.1	ZDHHC9	-3.1	PSAP	-3.2	LOC729444	-3.2
SPATA7	-3.1	HECTD2	-3.1	AK000420	-3.2	ANKRD10	-3.2
GON4L	-3.1	THC2588453	-3.1	ENST00000182096	-3.2	FLJ42627	-3.2
YIPF4	-3.1	LOC100192378	-3.1	TMEM181	-3.2	MAGEL2	-3.2
CDH22	-3.1	SLC1A4	-3.1	SNX16	-3.2	A_32_P79719	-3.2
C6orf168	-3.1	CB987747	-3.1	TMEM200B	-3.2	AK001057	-3.2
ZNF621	-3.1	THC2739159	-3.1	BG571904	-3.2	AK094629	-3.2
CFLAR	-3.1	PDE9A	-3.1	LINC00421	-3.2	ZNF251	-3.2
LOC441666	-3.1	RPS6KB1	-3.1	HOMER3	-3.2	DDX50	-3.2
RELB	-3.1	A_24_P358305	-3.1	EZH1	-3.2	AK091409	-3.2
HIST1H2BK	-3.1	AGTR1	-3.1	FAM21C	-3.2	ENST00000390539	-3.2

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
EDNRA	-3.2	LOC100653030	-3.3	SCN5A	-3.4	ADO	-3.5
ARL10	-3.2	A_24_P75558	-3.3	CCPG1	-3.4	RHOQ	-3.5
THC2733316	-3.2	U88896	-3.3	CALCRL	-3.4	MOXD1	-3.5
PPP1R15A	-3.2	SPDYE5	-3.3	NIPA1	-3.4	C1orf216	-3.5
TMSB15A	-3.2	MTHFR	-3.3	SLC37A1	-3.4	GPRC5C	-3.5
ABP1	-3.2	DGCR5	-3.3	DACT1	-3.4	INPP5K	-3.5
KCNK6	-3.2	SLC10A7	-3.3	ASPRV1	-3.4	ENST00000439259	-3.5
TTC17	-3.2	GLUL	-3.3	ANXA7	-3.4	C19orf6	-3.5
SRSF1	-3.2	GCLM	-3.3	COLEC12	-3.4	POU6F1	-3.5
C22orf31	-3.2	BC039411	-3.3	SYT15	-3.4	THC2710559	-3.5
AK055679	-3.2	THC2645667	-3.4	CYP4F12	-3.4	NFIB	-3.5
MME	-3.3	THC2648781	-3.4	ABCC8	-3.4	C4orf34	-3.5
FTH1	-3.3	SERINC2	-3.4	NEBL	-3.4	HLA-DPA1	-3.5
A_24_P850172	-3.3	MAFF	-3.4	SPAG9	-3.4	THC2549822	-3.5
SGMS1	-3.3	BX112754	-3.4	ENST00000461931	-3.4	BX091616	-3.5
LOC100130331	-3.3	FBXL7	-3.4	GOLIM4	-3.4	NPEPL1	-3.5
A_24_P281514	-3.3	AL834280	-3.4	CHMP4C	-3.4	A_32_P136063	-3.5
THC2521437	-3.3	PLAG1	-3.4	A_32_P187518	-3.4	RIPK2	-3.5
HSPA13	-3.3	GARNL3	-3.4	MME	-3.4	SPAG9	-3.5
ENST00000537552	-3.3	CNKSR3	-3.4	STBD1	-3.4	PDE4D	-3.5
SOX8	-3.3	BEND7	-3.4	STXBP5	-3.4	AMY1C	-3.5
MGC16121	-3.3	THC2513403	-3.4	AF339771	-3.4	C17orf51	-3.5
H2BFXP	-3.3	XIST	-3.4	FABP7	-3.4	TNFRSF21	-3.5
RHBDL3	-3.3	PPP3CA	-3.4	FAM160B1	-3.4	THC2650423	-3.5
FAT1	-3.3	DOCK4	-3.4	AK123096	-3.4	SMEK2	-3.5
BM147583	-3.3	PARVA	-3.4	ENST00000424587	-3.4	KIR2DS4	-3.5
MIR137HG	-3.3	AP1S2	-3.4	MYO15A	-3.4	ZNF23	-3.5
A_32_P31580	-3.3	DLEC1	-3.4	GAB3	-3.4	ME1	-3.5
HOXC10	-3.3	TNFAIP3	-3.4	DNAJB4	-3.4	CCDC165	-3.5
THC2668270	-3.3	A_24_P238819	-3.4	FAM196A	-3.4	COL4A6	-3.5
ENST00000340695	-3.3	PANX2	-3.4	ARMCX3	-3.4	PNMA3	-3.5
SLC44A3	-3.3	GTF2H5	-3.4	UCHL1	-3.4	ENST00000416395	-3.5
BC041996	-3.3	THC2701422	-3.4	CSRNP1	-3.4	LOC653061	-3.5
DPY19L4	-3.3	TMEM64	-3.4	EMX1	-3.4	TTLL7	-3.5
PLXDC2	-3.3	MMAB	-3.4	SEC63	-3.4	NFAT5	-3.5
A_24_P7494	-3.3	AKAP12	-3.4	LRRTM4	-3.4	ND6	-3.5
PHF10	-3.3	PLXNC1	-3.4	CHADL	-3.4	IFI27L2	-3.5
AK022183	-3.3	MMD	-3.4	FN1	-3.4	ENST00000445770	-3.5
C6orf70	-3.3	PANK3	-3.4	SENP6	-3.4	CXorf57	-3.5
FAM21A	-3.3	NAB2	-3.4	ZNF34	-3.4	JMJD1C	-3.5
AGAP7	-3.3	ALDH1A3	-3.4	MAP9	-3.4	ACE	-3.5

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
C12orf39	-3.5	MAFIP	-3.6	JHDM1D	-3.7	THC2520017	-3.8
ABCG4	-3.5	CTSZ	-3.6	KIF3C	-3.7	GAS6	-3.8
AFTPH	-3.5	THAP7-AS1	-3.6	LIG4	-3.7	WNT5B	-3.8
A_32_P149416	-3.5	PRKD1	-3.6	CTGF	-3.7	KLHDC1	-3.8
AI911586	-3.5	CASD1	-3.6	THC2679484	-3.7	TSPAN9	-3.8
DYSF	-3.5	MORC4	-3.6	ANO8	-3.7	LOC100132363	-3.8
AK091057	-3.5	THC2710703	-3.6	TIAM2	-3.7	SQLE	-3.8
BU618641	-3.5	AIFM3	-3.6	SGK1	-3.7	ACAT2	-3.8
THC2632286	-3.5	MAGEC1	-3.6	ENST00000411845	-3.7	THBD	-3.8
A_24_P92771	-3.5	A_24_P264413	-3.6	UFM1	-3.7	NARG2	-3.8
GGA1	-3.5	RASA4	-3.6	RFPL3-AS1	-3.7	GEM	-3.8
LIPG	-3.5	BAG3	-3.6	SLC2A13	-3.7	AZI2	-3.8
CBWD5	-3.5	CCDC126	-3.6	RNASET2	-3.7	UNC5B	-3.8
A_24_P170395	-3.5	ACTG1	-3.6	TLCD2	-3.7	DMP1	-3.8
A_32_P120211	-3.5	LOC100134167	-3.6	ULK2	-3.7	LOC148709	-3.8
SAMD4A	-3.5	GJA1	-3.6	RBM20	-3.7	PNMA3	-3.8
ANTXR2	-3.6	KIAA0513	-3.6	SLC30A5	-3.7	FAM153A	-3.8
A_32_P77178	-3.6	SAMD13	-3.6	TMEM200C	-3.7	PNMA2	-3.8
PRDM7	-3.6	LIMD2	-3.6	PERP	-3.7	BC028039	-3.8
A_24_P712193	-3.6	TSPAN7	-3.6	NRIP1	-3.7	SYT15	-3.8
RAB9B	-3.6	RBP1	-3.6	ZNF277	-3.7	SOX4	-3.9
UBE2O	-3.6	AK091744	-3.6	CLN8	-3.7	FAM164A	-3.9
INADL	-3.6	KCTD13	-3.6	BC029452	-3.7	A_32_P213543	-3.9
AV701505	-3.6	KCNMB4	-3.6	A_24_P650562	-3.7	AW627629	-3.9
ANTXR1	-3.6	A_32_P145302	-3.7	SH3PXD2A	-3.8	CBLB	-3.9
RTTN	-3.6	THC2702975	-3.7	BC034271	-3.8	SERPINE1	-3.9
NRIP3	-3.6	AK023394	-3.7	C1S	-3.8	ZNF853	-3.9
THC2544493	-3.6	THC2785860	-3.7	IFI44	-3.8	PCDH15	-3.9
MTRF1L	-3.6	TRPM3	-3.7	PLEKHA1	-3.8	LRP12	-3.9
A_23_P57836	-3.6	CROCCP3	-3.7	CHST11	-3.8	VMP1	-3.9
A_24_P298179	-3.6	MAFIP	-3.7	SUGT1P3	-3.8	BHLHE40	-3.9
A_32_P12282	-3.6	PRKCE	-3.7	THC2677037	-3.8	SPTBN5	-3.9
LRP12	-3.6	ENST00000551187	-3.7	TRIM23	-3.8	THC2655842	-3.9
VSTM4	-3.6	ATF3	-3.7	A_32_P157471	-3.8	A_24_P715434	-3.9
STOX2	-3.6	USP6	-3.7	CPA5	-3.8	TMEM18	-3.9
ZNF862	-3.6	A_32_P156628	-3.7	A_23_P73096	-3.8	PNPLA3	-3.9
TCP1	-3.6	FAM129A	-3.7	HNRNPR	-3.8	TMEM59L	-3.9
A_24_P148263	-3.6	RAB3C	-3.7	RSL1D1	-3.8	YPEL5	-3.9
COL27A1	-3.6	SLC45A4	-3.7	CCL27	-3.8	FAM135A	-3.9
HLA-DMA	-3.6	DNAJB4	-3.7	RTTN	-3.8	FST	-3.9
STMN3	-3.6	A_24_P681266	-3.7	ARHGEF2	-3.8	COL6A2	-3.9

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
GNAZ	-3.9	ENPP6	-4.0	PCDHB9	-4.1	NIPAL2	-4.2
ENST00000361201	-3.9	ZDHHC14	-4.0	ZNF684	-4.1	NFAT5	-4.2
MAP9	-3.9	HOXB13	-4.0	THC2637707	-4.1	A_32_P30898	-4.3
TMSB10	-3.9	PHF20L1	-4.0	KLF13	-4.1	CD302	-4.3
BF692226	-3.9	ENST00000479981	-4.0	IL17RA	-4.1	SLC7A3	-4.3
DKFZp761E198	-3.9	A_32_P112401	-4.0	ZNF471	-4.1	MAPT	-4.3
HSF2	-3.9	RFPL1-AS1	-4.0	A_24_P928453	-4.1	TTC7A	-4.3
PHF14	-3.9	C14orf149	-4.0	SIRPA	-4.1	AGAP7	-4.3
A_24_P383598	-3.9	SOCS3	-4.0	ZNF222	-4.1	CASC2	-4.3
C14orf37	-3.9	IGLL1	-4.0	A_32_P50508	-4.1	LINC00312	-4.3
BC033528	-3.9	VASH2	-4.0	HRC	-4.2	ITSN2	-4.3
TRIM9	-3.9	VSTM4	-4.0	A_32_P146450	-4.2	THC2544198	-4.3
COLQ	-3.9	WIPI1	-4.0	SYT15	-4.2	HSF2	-4.3
DENND2A	-3.9	BACE2	-4.0	ENST00000513644	-4.2	SSH3	-4.3
FTHL17	-3.9	C9orf131	-4.0	BQ050540	-4.2	RASD2	-4.3
AP4E1	-3.9	MMEL1	-4.0	FAM176A	-4.2	THC2681437	-4.3
GPR27	-4.0	LAMP3	-4.0	A_24_P273043	-4.2	HLA-DMA	-4.3
THC2635921	-4.0	HOXC10	-4.0	GALNT6	-4.2	AK124281	-4.3
GOLGA8A	-4.0	RAB32	-4.0	EXOSC6	-4.2	ARC	-4.3
ANXA2	-4.0	LOXL4	-4.0	IL12A	-4.2	EPHA3	-4.3
EGR4	-4.0	LOC390705	-4.0	ZC3H8	-4.2	HIF3A	-4.3
ENST00000487754	-4.0	LGALS12	-4.1	BQ674642	-4.2	CAST	-4.3
C20orf46	-4.0	THC2538610	-4.1	MGC23270	-4.2	LIMD2	-4.3
COL6A1	-4.0	BF217859	-4.1	A_32_P142363	-4.2	A_32_P141938	-4.3
GBE1	-4.0	SEL1L	-4.1	CR623787	-4.2	OBFC1	-4.3
PCYT1B	-4.0	AIF1	-4.1	ANXA5	-4.2	THC2560073	-4.3
MYCBPAP	-4.0	SEMA3C	-4.1	RNFT1	-4.2	KIF3C	-4.3
MXD1	-4.0	A_23_P204225	-4.1	ZNF222	-4.2	ZNF319	-4.3
TMSB4X	-4.0	A_24_P935852	-4.1	C17orf108	-4.2	CYP4F11	-4.3
KCNQ1	-4.0	FKBP1B	-4.1	PCDH18	-4.2	A_24_P409182	-4.3
SCUBE2	-4.0	SRSF12	-4.1	LINC00338	-4.2	IGIP	-4.3
DENND4A	-4.0	A_24_P452024	-4.1	CR594811	-4.2	ENST00000369381	-4.3
ETNK2	-4.0	AF090890	-4.1	GPR64	-4.2	C6orf70	-4.3
SGK223	-4.0	A_24_P530900	-4.1	AK124426	-4.2	SCN9A	-4.3
ENST00000504184	-4.0	MBNL3	-4.1	A_24_P127661	-4.2	GNG13	-4.3
GOLGA6L6	-4.0	TCF23	-4.1	LY6G5C	-4.2	ENST00000355232	-4.3
A_24_P631625	-4.0	A_32_P160670	-4.1	INSIG1	-4.2	CD302	-4.4
CD9	-4.0	SH3PXD2A	-4.1	DAGLA	-4.2	THC2614203	-4.4
ANG	-4.0	CD59	-4.1	DUSP13	-4.2	ENST00000421170	-4.4
AK025716	-4.0	TUSC1	-4.1	RNFT1	-4.2	SLC7A11	-4.4
A_32_P34372	-4.0	THC2535753	-4.1	C13orf15	-4.2	AOC3	-4.4

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ARHGAP44	-4.4	EYA4	-4.5	SNX9	-4.7	A_32_P73717	-4.9
PARP4	-4.4	CA13	-4.5	CCPG1	-4.7	SLC7A11	-4.9
TUSC1	-4.4	BG115931	-4.5	THC2661428	-4.7	PPM1K	-4.9
IGF2R	-4.4	C3orf80	-4.5	ENST00000518339	-4.7	SRSF8	-4.9
GPR161	-4.4	GPR155	-4.5	RBM11	-4.7	COL4A3	-5.0
LOC100129196	-4.4	TTC18	-4.5	BACE2	-4.7	MYBL1	-5.0
MXRA8	-4.4	ZBTB1	-4.5	ENST00000390636	-4.7	THC2753968	-5.0
INPP4B	-4.4	THC2729109	-4.5	BM926140	-4.7	ENST00000417781	-5.0
ZNF432	-4.4	MALAT1	-4.5	A_24_P914669	-4.7	IL11	-5.0
LOC100131053	-4.4	FAM129A	-4.5	B4GALNT3	-4.8	SOX7	-5.0
GOLGA8F	-4.4	LOC100499466	-4.6	TMSB4X	-4.8	A_24_P357933	-5.0
A_24_P587993	-4.4	TSEN54	-4.6	A_24_P928031	-4.8	ABCA5	-5.0
HOXA2	-4.4	THC2515382	-4.6	MYB	-4.8	FAM59B	-5.0
THC2532166	-4.4	AF257098	-4.6	C11orf96	-4.8	PMP22	-5.0
A_32_P98914	-4.4	NDUFA4L2	-4.6	MTHFD2L	-4.8	A_32_P40673	-5.0
MYO15B	-4.4	CTAGE1	-4.6	CCPG1	-4.8	WIPF1	-5.0
LOC100506686	-4.4	TBX21	-4.6	TTC39A	-4.8	COL5A1	-5.1
LYST	-4.4	LINC00304	-4.6	THC2481891	-4.8	GGT7	-5.1
UPK3A	-4.4	A_23_P393495	-4.6	MALAT1	-4.8	A_23_P251002	-5.1
AK025975	-4.4	SPARCL1	-4.6	HIST1H3I	-4.8	NECAB1	-5.1
NAIP	-4.4	NKAIN1	-4.6	PDE4DIP	-4.8	TRIM7	-5.1
CACNA1D	-4.4	MAP3K14	-4.6	DOCK4	-4.8	CXorf57	-5.1
DSCR6	-4.5	AP4E1	-4.6	LCP1	-4.8	TNFAIP8L3	-5.1
FOXD4	-4.5	DHDH	-4.6	TSC22D3	-4.8	A_24_P923510	-5.1
TSPAN12	-4.5	THC2685727	-4.6	TCAM1P	-4.8	KPNA5	-5.1
AL574249	-4.5	BEND6	-4.6	MOCOS	-4.8	TPBG	-5.1
MMP16	-4.5	LPIN1	-4.6	TBXAS1	-4.8	CCDC40	-5.1
WIPF1	-4.5	ZDHHC14	-4.6	DHX34	-4.8	ZNF642	-5.1
IFIT5	-4.5	TMEM87B	-4.6	SMOX	-4.8	STOX2	-5.1
FLJ42709	-4.5	SPHK1	-4.6	THC2740861	-4.8	HOXC13	-5.1
MGC23284	-4.5	HLA-DPB1	-4.6	QKI	-4.8	DOK6	-5.1
SPAG1	-4.5	SASH1	-4.6	C12orf68	-4.9	THC2686110	-5.1
A_24_P578445	-4.5	COL12A1	-4.7	EPHA3	-4.9	GOLGA6A	-5.2
SH3BP5	-4.5	THC2728570	-4.7	PRPH	-4.9	CEACAM19	-5.2
RPS6KB1	-4.5	BX114143	-4.7	PDE4DIP	-4.9	A_32_P134556	-5.2
ESF1	-4.5	RNF157	-4.7	A_23_P421323	-4.9	TUBB8	-5.2
RSPH3	-4.5	A_24_P187154	-4.7	H6PD	-4.9	BQ064481	-5.2
OGFRL1	-4.5	SNX9	-4.7	INPP1	-4.9	HES2	-5.2
SLC16A9	-4.5	TDRD10	-4.7	KCTD12	-4.9	TSPAN32	-5.2
TLE1	-4.5	DYNLT3	-4.7	AKAP12	-4.9	TRAF3IP2	-5.2
PRSS35	-4.5	SLC10A4	-4.7	LOC388630	-4.9	FLJ90757	-5.2

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SLCO5A1	-5.2	C13orf15	-5.4	FYN	-5.7	DAAM1	-6.1
KLF2	-5.2	RUNX3	-5.4	VILL	-5.7	FOXE1	-6.1
ARRDC3	-5.2	A_23_P108534	-5.4	FOSL1	-5.8	A_32_P220912	-6.1
RBM24	-5.2	A_24_P204257	-5.4	FIGF	-5.8	REEP3	-6.2
BG682198	-5.2	RHCE	-5.4	STXBP5	-5.8	CPN2	-6.2
TTLL7	-5.2	RAB30	-5.4	TSPAN5	-5.8	ATP10A	-6.2
ZNF184	-5.2	HMGCR	-5.5	THC2644672	-5.8	FGD5	-6.2
MAP3K1	-5.2	SRRM3	-5.5	THC2651324	-5.8	PPM1L	-6.2
TRAM1L1	-5.2	THC2642650	-5.5	A_24_P746044	-5.8	USP32P1	-6.2
TBC1D3B	-5.2	A_24_P917810	-5.5	RPL23AP32	-5.8	LIPA	-6.2
A_24_P144149	-5.2	GNL1	-5.5	NUAK1	-5.8	LOC100499177	-6.2
SFTPA1	-5.2	A_23_P141785	-5.5	NIN	-5.8	HMGCS1	-6.2
TAC3	-5.2	CD46	-5.5	A_23_P46070	-5.9	SQSTM1	-6.2
MOCOS	-5.2	COL3A1	-5.5	ST18	-5.9	FHOD3	-6.2
A_32_P145159	-5.2	DEM1	-5.5	MAP9	-5.9	PURG	-6.2
LOC554207	-5.2	REEP3	-5.5	HOXC12	-5.9	AHNAK	-6.2
LRRC10B	-5.2	A_32_P85578	-5.5	AK027319	-5.9	BX537819	-6.3
A_24_P315885	-5.2	ANXA1	-5.5	PLAC9	-5.9	ENST00000513644	-6.3
DST	-5.2	RECQL	-5.5	SMAGP	-5.9	MOB3B	-6.3
CCR3	-5.3	THC2687042	-5.5	POFUT1	-5.9	THSD1	-6.3
FGF7	-5.3	DYNLT3	-5.5	ETNK2	-5.9	LRRCC1	-6.3
MGAT5B	-5.3	DUSP8	-5.5	CEP104	-5.9	ZNF222	-6.3
LOC728431	-5.3	HECA	-5.5	UBL4B	-5.9	FOXE1	-6.4
ANTXR1	-5.3	AK021593	-5.5	AF116619	-5.9	F7	-6.4
ZFYVE28	-5.3	TRPM7	-5.6	ADAM23	-5.9	CLIP2	-6.4
RGS20	-5.3	A_24_P940079	-5.6	NDRG1	-6.0	PABPC1L	-6.4
SPINK2	-5.3	PTPRH	-5.6	LOC284454	-6.0	MXD1	-6.4
LOC286382	-5.3	BC017350	-5.6	C17orf76	-6.0	SYCP2	-6.4
LOC157562	-5.3	THC2664573	-5.6	MIR22HG	-6.0	BM695552	-6.4
NRG2	-5.3	A_23_P91130	-5.6	KAT2B	-6.0	RRAGD	-6.4
A_32_P23872	-5.3	ATP1B1	-5.6	TMEM130	-6.0	THC2657737	-6.5
AMZ2P1	-5.4	SYCP3	-5.6	ENST00000460407	-6.0	TMEM155	-6.5
A_32_P96752	-5.4	ETS2	-5.6	APLF	-6.0	LMF1	-6.5
EMILIN2	-5.4	POM121L8P	-5.6	TRIM9	-6.0	MALAT1	-6.5
LOC100127983	-5.4	REEP3	-5.7	THC2543854	-6.0	PRKCA	-6.5
BMS1P1	-5.4	CHRD	-5.7	A_24_P281264	-6.0	COL3A1	-6.5
A_24_P212997	-5.4	HMGCS1	-5.7	LOC643802	-6.1	LRRCC1	-6.5
DDIT3	-5.4	THC2525505	-5.7	AL049260	-6.1	LOC388796	-6.5
THC2643957	-5.4	NR2F2	-5.7	GOLGA8E	-6.1	TOX2	-6.6
PLA2G2F	-5.4	ANKRD6	-5.7	ATP1B1	-6.1	A_24_P771821	-6.6
LGI4	-5.4	LOC497257	-5.7	RNF217	-6.1	PARVA	-6.6

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ZFP37	-6.6	BEGAIN	-7.3	ATRNL1	-8.0	C11orf41	-8.8
BG216262	-6.6	MBNL2	-7.3	SLC45A1	-8.0	WNK4	-8.8
SRGAP1	-6.6	CAMTA1	-7.4	CPAMD8	-8.0	TUBB3	-8.8
PADI4	-6.6	SLC17A5	-7.4	A_32_P327750	-8.1	RNF217	-8.8
A_32_P226656	-6.6	EDNRA	-7.4	SYNE1	-8.1	FNDC4	-8.8
MSMO1	-6.7	PLGLB1	-7.4	NOS2	-8.1	PRSS16	-8.9
C18orf1	-6.7	TRIML2	-7.4	FAM101A	-8.1	AK123861	-9.0
CLIP4	-6.7	SDK2	-7.4	COL1A1	-8.1	ATL1	-9.0
AI669333	-6.7	JAKMIP3	-7.4	SYT17	-8.1	A_24_P401521	-9.0
COL5A1	-6.7	BC031314	-7.4	BQ717518	-8.1	SYCP2	-9.0
LRFN5	-6.8	SLC7A11	-7.4	TGFBI	-8.1	SLC30A3	-9.1
TRPM7	-6.8	ITGBL1	-7.4	LIF	-8.2	WDR17	-9.1
FAM101A	-6.8	RGMA	-7.4	AI732190	-8.2	SPAG1	-9.1
A_23_P384355	-6.8	CSGALNACT2	-7.5	SPAG9	-8.2	OSTF1	-9.1
PBX1	-6.9	ATF3	-7.6	TTC39C	-8.3	TSHZ3	-9.1
TGFBR2	-6.9	PLK2	-7.6	BC037919	-8.3	LOC349196	-9.3
GALNT3	-6.9	DOK6	-7.6	VSTM4	-8.3	CACHD1	-9.3
KIAA0226L	-6.9	AK074562	-7.6	SYT15	-8.3	C9orf95	-9.3
KAZN	-6.9	FEZ1	-7.6	CAMK2N1	-8.3	KIAA1377	-9.3
PLVAP	-7.0	PTGIS	-7.7	DENND2C	-8.4	LOC728392	-9.4
LAMB1	-7.0	THC2693741	-7.7	GNG2	-8.4	NEAT1	-9.4
CAMK2N1	-7.0	C6orf145	-7.7	A_23_P95125	-8.4	IL6R	-9.4
HHAT	-7.0	SOX4	-7.7	SYNE1	-8.4	RHOBTB3	-9.5
ITGAV	-7.0	ENST00000462693	-7.7	DENND1B	-8.4	ST3GAL6	-9.7
NAIP	-7.0	TMCC2	-7.7	A_32_P138939	-8.4	ENST00000485253	-9.7
PLAGL1	-7.0	EGR1	-7.8	MALAT1	-8.4	MIRLET7BHG	-9.7
CBLB	-7.0	ANTXR1	-7.8	RUFY2	-8.5	A_32_P173922	-9.7
ENST00000439362	-7.1	JAKMIP1	-7.8	MTMR11	-8.5	A_24_P229726	-9.8
NEAT1	-7.1	KBTBD11	-7.8	CRYBA2	-8.5	BC037919	-9.8
PAG1	-7.1	RNASE4	-7.8	A_24_P25040	-8.5	PRSS12	-9.9
THC2660361	-7.2	DAAM1	-7.8	EPB41L3	-8.6	A_24_P920715	-9.9
ZNF704	-7.2	DLX4	-7.8	PKNOX2	-8.6	TTC39C	-9.9
KCTD14	-7.2	SMPDL3A	-7.8	AHNAK	-8.6	PTPN3	-10.0
DENND1B	-7.2	MMP10	-7.8	HIVEP3	-8.6	ZFYVE28	-10.0
ENST00000440990	-7.2	OLFML3	-7.9	PPP2R2C	-8.6	AW118118	-10.0
THC2503300	-7.2	ATAD3B	-7.9	TMEM87B	-8.6	CR594811	-10.0
LOC653061	-7.2	FSTL5	-7.9	CCKBR	-8.7	FXYD1	-10.0
PFKFB3	-7.2	KIAA1751	-7.9	EPAS1	-8.7	SCIN	-10.0
ATRNL1	-7.2	COL3A1	-7.9	MAP6	-8.7	GABARAPL1	-10.0
OLFML3	-7.2	LRRC4C	-8.0	KIAA1147	-8.7	AK094289	-10.3
GPC5	-7.3	KLF6	-8.0	GRID1	-8.8	GPR84	-10.3

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
PRSS23	-10.3	SRPX	-13.2	MAGI2	-17.2	JUN	-25.3
LACC1	-10.3	CRLF1	-13.2	AF222023	-17.2	ENST00000517562	-25.8
NR2F2	-10.4	QKI	-13.3	ZNF704	-17.3	EGR2	-26.5
C6orf168	-10.4	HIPK2	-13.3	RIPPLY2	-17.5	AF100640	-26.7
A_23_P139166	-10.4	LGI2	-13.3	SCN7A	-17.6	CHST15	-27.4
CA13	-10.4	JAK1	-13.4	AY227436	-17.6	SH3GL3	-27.9
ELL2	-10.5	SC5DL	-13.4	GCLC	-17.7	MYOF	-28.0
LOC389634	-10.7	PRAMEF8	-13.8	TSPAN5	-17.9	KIAA0319	-28.7
EYA4	-10.7	LONRF2	-13.8	TGFB2	-18.3	PPIC	-28.9
LOC100127983	-10.8	PRDM13	-13.9	PLEKHG4	-18.4	KIF26B	-29.1
LPIN1	-10.8	HIPK2	-14.0	ACSS1	-18.6	LHX2	-29.2
FEZ1	-10.8	IRS2	-14.0	ASB5	-18.6	AB014766	-30.4
CELF6	-10.8	RNF144A	-14.0	AF264627	-18.6	TMEM98	-31.1
BG428517	-11.0	RTN1	-14.0	F10	-18.7	ADAM23	-32.9
GABARAPL1	-11.0	PTH1R	-14.1	PAPPA	-18.8	HOXB13	-34.1
TM4SF1	-11.0	PAPPA	-14.1	IRX4	-18.8	AR	-34.1
SATB2	-11.1	FAM43B	-14.1	ROBO2	-19.0	TMEM98	-34.3
GABARAPL3	-11.3	SC5DL	-14.2	STYK1	-19.2	A_32_P168756	-35.1
ENST00000537659	-11.7	SC5DL	-14.2	CDK6	-19.6	EGR3	-35.9
A_24_P597242	-11.7	F2RL2	-14.5	PTPN3	-19.6	DACT1	-36.2
RFTN1	-11.8	GDF10	-14.7	TUBB2B	-19.6	MYOF	-36.9
P2RY1	-11.8	AUTS2	-14.7	KRT80	-19.7	CYP26B1	-37.4
MDGA1	-11.8	EMILIN1	-14.7	RNF128	-20.2	HTRA1	-39.0
PAG1	-11.9	BICD1	-14.8	RNF150	-20.3	TBX15	-40.2
THC2642212	-12.0	DUSP8	-14.8	HOPX	-20.4	ARNT2	-42.0
NAP1L2	-12.1	FOXD2	-14.9	HTRA3	-21.0	HSPA12A	-44.2
AW964144	-12.1	LARGE	-15.2	ANKRD33B	-21.4	FOXD1	-45.0
ZDBF2	-12.1	MKL2	-15.2	PPIC	-21.5	EPDR1	-47.5
BE612504	-12.2	MYL3	-15.3	TTC39C	-21.7	A2M	-48.3
CLN8	-12.2	HIPK2	-15.3	SLC7A10	-21.7	IGF2	-48.7
HIPK2	-12.4	KIAA1377	-15.3	AF264621	-21.8	JAM2	-49.3
ENST00000318245	-12.4	ROBO2	-15.4	LOC100132593	-22.3	MMP16	-49.9
ITM2A	-12.5	PRSS23	-15.7	B3GNT5	-22.4	MYOF	-52.3
SPP1	-12.5	RNF128	-15.7	HMOX1	-22.7	ST3GAL1	-55.1
LMCD1	-12.5	TDRD3	-15.9	GLT1D1	-22.9	ZNF469	-55.7
TGFB2	-12.6	CPE	-15.9	CH25H	-23.0	C11orf41	-55.9
SRGN	-12.8	L3MBTL3	-16.2	SLC22A15	-23.6	FNDC1	-56.6
AMOTL1	-12.8	AF363068	-16.3	CALB1	-23.6	DB534761	-64.8
TTC39C	-12.9	A_32_P171200	-16.4	UST	-23.9	KLHL29	-68.0
L3MBTL3	-13.1	KIF5C	-16.6	EFNA5	-24.5	CNRIP1	-68.6
BAI3	-13.1	ZNF704	-16.7	GCLC	-24.7	ROBO2	-68.7

Appendix VII Gene Expression Changes in $A2780_{DXL\text{-}CBN}$ vs. $A2780_{CBN}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
GDF10	-69.0						
ST3GAL1	-70.2						
JAM2	-75.2						
SPATS2L	-80.8						
IQGAP2	-85.8						
F2R	-86.9						
A_23_P123234	-88.6						
GALNT14	-188.4						
ENOX1	-796.5						

Appendix VIII Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
PCDH20	675	LOC100132735	72.1	RERGL	33.1	THC2610890	18.6
AF264621	543	HECA	71.0	GSTO2	33.0	TMEM100	18.1
LUM	535	BF217859	69.9	STAMBPL1	32.8	FAS	18.0
PPP4R4	493	LOC285141	69.6	CA2	32.3	BEGAIN	17.7
AY227436	350	LGALS3	68.3	THC2535223	32.3	P2RY1	17.6
AF100640	265	LINC00470	61.9	GAD1	31.8	BACH2	17.4
GAD1	213	CU675110	61.1	IGF1R	31.5	CU675788	17.2
FOXG1	197	SLITRK1	60.3	PCDHB5	30.3	A_32_P41594	17.0
MGAT4C	195	DLC1	57.6	MYLIP	30.1	DLK1	16.8
ANXA10	192	PDZRN4	55.2	PTPRK	29.7	A_24_P401521	16.7
TACSTD2	185	PLAC8	54.1	KCNMA1	29.3	FZD1	16.6
KANK1	170	ASB9	51.8	MLKL	28.6	GPC4	16.6
METTL7A	168	ATRNL1	51.6	MCF2	27.9	A_32_P72541	15.5
MLH1	167	DOK6	50.9	MDK	27.9	MPPED2	15.5
HTATIP2	163	SLITRK1	50.8	EFNB2	27.4	LGI2	14.9
BEX1	162	LINC00470	49.8	IDO1	26.7	C8orf4	14.9
A_24_P920715	161	LUM	49.1	SP5	26.2	PPP3CA	14.4
DMRT3	161	HAPLN1	47.7	SPP1	25.5	HOXD10	14.4
C8orf4	154	CD109	47.2	SP7	25.2	RERG	14.4
AB014766	147	ABCA5	47.2	OVOL2	25.1	PALMD	14.3
CELF2	146	RASSF9	45.4	RUNDC3B	25.0	GLCCI1	14.3
CBR1	141	BEX2	45.4	SPOCK3	24.6	CBR3	14.2
LHX2	132	ABCA5	45.4	RARB	24.2	JAM2	14.2
DNAJC15	110	C14orf23	43.7	DCDC5	23.7	BF217859	13.9
EPCAM	108	SGCG	43.1	DNAJC12	23.5	JUN	13.8
TOX	100	NFIA	42.8	CGREF1	23.3	IDO2	13.5
LRP1B	94.6	HS3ST3A1	41.4	MLKL	22.0	THC2512148	13.3
DOCK4	94.5	OTP	41.3	THC2730631	21.8	C1orf173	13.3
DCN	93.4	SLITRK6	41.1	MSX2	21.8	EIF4E3	13.2
ATRNL1	91.6	DOK6	40.8	GLCCI1	21.3	LMO4	13.0
HS3ST3B1	88.1	LOC100505806	40.2	SPON2	21.0	PCDH18	12.9
ANKRD22	87.2	PBX1	39.8	TBX18	20.8	CU675508	12.6
DMRT1	83.8	HTATIP2	39.6	PAX6	20.7	L3MBTL3	12.6
FAM198B	82.3	RIN2	39.2	PBX1	19.7	RFTN2	12.5
TOX	78.3	CBR3	38.4	CDCA7L	19.5	RGS20	12.4
TMEM26	78.2	ARHGDIB	38.4	ABCB1	19.5	SNTG1	12.4
CYB5A	76.3	SGCE	37.4	PTN	19.2	PRTFDC1	12.3
VGLL3	75.7	CALCA	36.3	CD247	19.1	PAPSS2	12.2
NTS	73.7	FOXP1	35.9	ERP27	19.0	A_32_P210193	12.2
PLAC8	72.4	SFRP1	35.4	THC2696414	18.8	ANXA1	12.1
		KANK1	33.4	CR936711	18.7	COL1A2	12.1

Appendix VIII Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
TLE1	12.0	IFI27L2	9.3	ANKRD20A2	7.0	THC2712710	5.8
CNTNAP2	12.0	NR2F2	9.2	FAM82A1	7.0	MIOS	5.8
TBX15	12.0	NPR2	9.2	LOC375295	6.9	FAM169A	5.8
SLC13A3	12.0	DSCR6	9.1	MAP2K6	6.9	PROC	5.8
CTNNA3	11.7	KCNMA1	9.0	CASP10	6.8	RRAGD	5.8
ENST00000514673	11.5	CD226	8.9	TP53TG1	6.8	PLCH1	5.7
ICA1	11.5	SMAD9	8.9	BAALC	6.8	BTG1	5.7
A_24_P910080	11.5	FERMT1	8.9	RGS11	6.8	NCAM2	5.7
PRR16	11.4	RTTN	8.8	ISOC1	6.8	A_24_P733345	5.7
THC2663361	11.4	SCHIP1	8.7	EFHC2	6.7	DYNLT3	5.7
SCRG1	11.4	MAP2K6	8.6	ATP6V0D2	6.7	ME1	5.7
MAOB	11.2	FUT4	8.5	CCDC3	6.7	TTC39A	5.6
WNT5B	11.0	PAPSS2	8.4	C9orf95	6.7	LOC100132167	5.6
TLX1	11.0	DB381305	8.4	CDS1	6.6	KIAA1147	5.5
FAM46A	10.9	MNS1	8.3	STON1	6.6	ME1	5.5
CD109	10.7	CTSF	8.3	RHOH	6.6	STOX2	5.5
BTNL2	10.7	HAND2	8.3	LOC100505938	6.5	SLC16A14	5.5
CU690253	10.7	CHRNA3	8.3	FAM82A1	6.5	CNTNAP3B	5.5
ADAM23	10.7	SNX7	8.3	SMAD9	6.5	PITX1	5.5
SCIN	10.7	FOXN4	8.2	LTK	6.4	BG695979	5.4
LOC375295	10.7	TNNI3K	8.2	ATL1	6.4	MDFI	5.3
RBM47	10.6	GSTM4	8.1	C4orf49	6.4	CAST	5.3
CYB5R2	10.5	GCH1	8.1	SC5DL	6.3	ODZ3	5.3
A_32_P179317	10.4	NEFL	7.9	PDZD2	6.3	ZNF630	5.3
THC2586657	10.4	FAM5C	7.8	FAM169A	6.3	CASP10	5.3
THC2679424	10.4	BEND6	7.8	ATP6V0D2	6.3	PPP1R3D	5.2
GLIS1	10.3	FGF9	7.7	GPC3	6.3	STXBP5L	5.1
GSTM4	10.3	ANKRD20A2	7.7	TMTC1	6.2	FAM7A1	5.1
BMPER	10.2	GUCY1A3	7.5	DZANK1	6.2	GSTM4	5.1
CRYBA2	9.9	THC2744399	7.5	ODZ3	6.2	ITGA1	5.1
LHFP	9.9	MLLT3	7.5	GSTM1	6.1	ATP11C	5.1
CITED2	9.9	MDGA1	7.5	TRIB2	6.1	MIOS	5.0
CA13	9.9	TP53TG1	7.4	C7orf31	6.0	THC2704911	5.0
MMRN1	9.9	IRS2	7.3	OXR1	6.0	ENST00000521369	5.0
SULF1	9.9	ENST00000537149	7.3	TFPI	6.0	ZNF462	5.0
CARD18	9.6	STOX2	7.2	ATP1B1	5.9	OSTF1	4.9
MGP	9.6	A_32_P222241	7.2	PDE3A	5.9	FBXO8	4.9
S1PR1	9.5	LOC90499	7.1	SEMA5A	5.9	COL2A1	4.9
P2RX5	9.5	NCAM2	7.1	DYNLT3	5.9	SGK3	4.9
PTPN21	9.5	ATP1B1	7.1	SC5DL	5.9	LOC400099	4.9
BC037328	9.4	MLH3	7.1	SLC3A1	5.8	CAST	4.8

Appendix VIII Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
GSTM2	4.8	GNG2	4.0	GPER	3.5	OPN3	3.1
OXR1	4.8	CEP44	4.0	B4GALT1	3.5	OXR1	3.1
CEP44	4.8	SLMO2	4.0	RGL1	3.5	ASF1A	3.1
SSPN	4.8	PCDHB16	4.0	RCAN3	3.5	SETD4	3.1
RHOBTB3	4.8	RND3	4.0	CHGB	3.5	A_32_P99804	3.1
DZANK1	4.8	CITED1	3.9	NDE1	3.5	GPR126	3.1
AK124097	4.7	THC2525505	3.9	GSTM5	3.4	TMX4	3.1
SLC27A6	4.7	STEAP1	3.9	LOC729852	3.4	LOX	3.1
RBAK-LOC389458	4.7	MGC45800	3.9	FSTL1	3.4	PUS7L	3.0
SLC7A10	4.7	ARHGEF4	3.9	SIRT1	3.4	A_24_P832737	3.0
CHODL	4.7	IRAK4	3.8	A_32_P233727	3.4	BLVRA	3.0
ME1	4.6	MBNL2	3.8	C4orf33	3.4	DEPDC7	3.0
SHD	4.6	DTX3	3.8	TTC8	3.4	BRP44L	3.0
B3GNT5	4.6	PCDHB8	3.8	UBR3	3.4	LOC100144602	3.0
STK17A	4.6	THC2643084	3.8	EMILIN3	3.3	HDDC2	3.0
HEBP2	4.5	TMTC1	3.8	DLK2	3.3	OMA1	3.0
AGL	4.5	ATP11C	3.7	GRHL3	3.3	HOXD9	3.0
PCDHGA3	4.5	MYB	3.7	THC2704459	3.3	C1orf173	3.0
MBOAT1	4.4	RNLS	3.7	PTEN	3.3	SOBP	3.0
PRKAR2B	4.4	PPP2R2B	3.7	COL3A1	3.3	LRP11	3.0
ZDHHC8P1	4.4	KCTD1	3.7	ASPRV1	3.3	SOCS6	3.0
THC2655527	4.4	NR2F2	3.7	CNTNAP3B	3.2	COL3A1	3.0
TMEM26	4.4	PEX1	3.7	ICK	3.2	SPATA13	3.0
IL28RA	4.4	TUBB2B	3.7	FRZB	3.2	UBR3	3.0
STEAP1	4.3	FAM160B1	3.7	BC014971	3.2	A_32_P212764	3.0
THC2639689	4.3	A_32_P145477	3.7	DSE	3.2	C6orf48	3.0
HOXD8	4.3	CLIP4	3.7	OMA1	3.2	A_32_P120211	2.9
DCLK1	4.3	OLFM3	3.7	GEM	3.2	TSPYL4	2.9
RCAN3	4.2	GNAS	3.6	SLC38A4	3.2	ASF1A	2.9
CCDC80	4.2	SEMA6D	3.6	C6orf204	3.2	RNF152	2.9
CD302	4.2	ACTA2	3.6	MIRLET7BHG	3.2	ADD3	2.9
DZANK1	4.2	SDCBP2	3.6	ZNF37BP	3.2	DCBLD1	2.9
ANKRD6	4.2	NMUR1	3.6	ENST00000420759	3.2	ZBTB8A	2.9
FNDC4	4.2	ERLIN2	3.6	FAM168A	3.2	TRIM2	2.9
A_24_P871726	4.2	BHLHE41	3.6	HFE	3.2	TUB	2.9
AUTS2	4.2	WDR25	3.6	COL3A1	3.1	FOXN3	2.9
FREM1	4.1	BX648207	3.6	PTEN	3.1	SNX29	2.9
THC2524341	4.1	C6orf204	3.6	ENST00000433980	3.1	TMEM22	2.9
AGPHD1	4.0	BCHE	3.5	RGS13	3.1	ENST00000437190	2.9
STEAP1	4.0	ANKRD20A5P	3.5	TMEM117	3.1	ADD3	2.9
MCOLN2	4.0	GNAS	3.5	BAMBI	3.1	THC2785860	2.9

Appendix VIII Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SLC12A2	2.9	THC2656479	2.6	DOK7	2.5	FGFR1OP	2.3
CLASP2	2.9	CCDC74B	2.6	ITPKB	2.5	MGAT5B	2.3
BC019907	2.8	NT5DC1	2.6	STMN3	2.5	CCNC	2.3
ISL1	2.8	FAM101A	2.6	DLEU2	2.5	LOC220906	2.3
SLMO2	2.8	MBD5	2.6	GTF2IRD1	2.5	FKBP7	2.3
DMKN	2.8	GUSBP4	2.6	ZNF345	2.5	BC000986	2.3
TMEM22	2.8	AKAP9	2.6	AK075186	2.5	CHDH	2.3
TUBA3C	2.8	KLHL14	2.6	POPDC3	2.5	PRIM2	2.3
C9orf125	2.8	ZBTB8A	2.6	PEX6	2.5	SNX9	2.3
GLYATL1	2.8	SLC16A9	2.6	CHRNA5	2.5	NT5DC1	2.3
ZNF184	2.8	IFI27L1	2.6	VCX2	2.4	ADAT2	2.3
PEX3	2.8	THC2664860	2.6	ACTR3BP2	2.4	COX6B2	2.3
CPE	2.8	ENST00000520259	2.6	SRSF12	2.4	KLF9	2.3
DGAT2	2.8	CDC40	2.6	AK130366	2.4	FAM50B	2.3
SLC40A1	2.8	GNAS	2.6	TJP2	2.4	A_32_P174385	2.3
CCDC28A	2.8	TTC7A	2.6	PTEN	2.4	FRMD4A	2.3
ZNF76	2.8	AK094629	2.6	REPS1	2.4	ENST00000436263	2.3
BI836406	2.8	MMD	2.6	CABYR	2.4	ZUFSP	2.3
CD302	2.7	Z69892	2.6	MMS22L	2.4	A_24_P528213	2.3
THC2554861	2.7	RASD1	2.6	CDC40	2.4	PLK1S1	2.3
STK17B	2.7	RBP1	2.6	MGC16121	2.4	C7orf50	2.3
A_32_P205139	2.7	C6orf89	2.6	ECHDC2	2.4	C20orf177	2.3
ULK2	2.7	NT5M	2.6	EML4	2.4	ZC3H6	2.3
GLRX	2.7	TMX4	2.6	KAZALD1	2.4	LOC254057	2.2
BACE1	2.7	TMEM35	2.6	C1GALT1	2.4	URGCP	2.2
CCDC74B	2.7	CU679836	2.5	RAB11FIP4	2.4	CENPW	2.2
ST7-AS1	2.7	MLLT11	2.5	AK021866	2.4	GOPC	2.2
TMC7	2.7	ACAT2	2.5	RWDD1	2.4	FAM126A	2.2
SESN1	2.7	C9orf125	2.5	ACTR3B	2.4	CUL7	2.2
EXOC2	2.7	KIAA1522	2.5	GTF2IRD1	2.4	EML4	2.2
ABLIM1	2.7	LOC100507568	2.5	SERPINB1	2.4	POLD2	2.2
MGC16703	2.7	C1orf53	2.5	UBAP1L	2.4	SAP30	2.2
CHN1	2.7	THC2646608	2.5	SAMD11	2.4	A_23_P122650	2.2
RTDR1	2.7	TLE2	2.5	THC2621221	2.4	TRIM4	2.2
FDX1	2.7	C6orf26	2.5	CSRP2	2.4	CEP41	2.2
SLC7A8	2.7	IFNGR1	2.5	VTA1	2.4	SLC25A40	2.2
STK17B	2.7	ACAT2	2.5	OXR1	2.4	C11orf70	2.2
DEM1	2.7	ACTR3B	2.5	ZP3	2.4	C1orf52	2.2
TUBB8	2.7	CPT1A	2.5	A_24_P170357	2.4	CTNNBIP1	2.2
EPHA3	2.7	DGAT2	2.5	FBLN7	2.4	ST7	2.2
ITGB5	2.6	FOXN3	2.5	EFCAB1	2.3	CDC40	2.2

Appendix VIII Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
CENPW	2.2	SLC25A29	2.1	SMO	2.1	LEMD2	2.0
FBXO5	2.2	AY090769	2.1	SDCBP	2.1	RFFL	2.0
SPARCL1	2.2	FBN1	2.1	THC2608799	2.1	CPNE5	2.0
RPL7L1	2.2	CD70	2.1	PTPN6	2.1	KIAA1586	2.0
FKBPL	2.2	PEX7	2.1	PLA2G12A	2.1	TRPM4	-2.0
EIF3F	2.2	C20orf201	2.1	DLX6	2.1	BCL3	-2.0
ARID5B	2.2	TRIM6	2.1	AGAP3	2.1	RASSF2	-2.0
SNTA1	2.2	C10orf118	2.1	SENP6	2.1	COL23A1	-2.0
VASH2	2.2	CDC40	2.1	LOC100133091	2.1	ARID3A	-2.0
FKBP1B	2.2	ENST00000456460	2.1	PIGS	2.1	C15orf59	-2.0
ENST00000435913	2.2	A_24_P24806	2.1	TMEM181	2.1	GGH	-2.0
EMID1	2.2	KCNMB3	2.1	ST7	2.1	RAB6B	-2.0
CHST6	2.2	ENST00000435913	2.1	MYH3	2.1	PCK2	-2.0
A_24_P780609	2.2	C6orf70	2.1	IBTK	2.1	ENST00000542925	-2.0
A_24_P409471	2.2	SHPRH	2.1	C6orf115	2.1	CCND2	-2.0
SRSF12	2.2	A_24_P323916	2.1	PSMB1	2.1	ITGB1	-2.0
A_24_P374973	2.2	GSTA4	2.1	PCMT1	2.1	COL1A1	-2.0
MGST2	2.2	TUSC1	2.1	RNF146	2.0	VEGFC	-2.0
A_24_P409697	2.2	AK023086	2.1	KCNQ2	2.0	RGPD5	-2.0
ACOT13	2.2	ENST00000518481	2.1	ZNF277	2.0	THC2632823	-2.0
A_32_P190334	2.2	A_24_P324644	2.1	C12orf60	2.0	SEPW1	-2.0
A_24_P290263	2.2	A_24_P341489	2.1	A_24_P288993	2.0	WARS	-2.0
ARID5B	2.2	JARID2	2.1	ENST00000378432	2.0	FBLIM1	-2.0
KIAA1009	2.2	THC2693923	2.1	GTF2I	2.0	AJUBA	-2.0
A_32_P162939	2.2	MDH2	2.1	PCMT1	2.0	EFHA2	-2.0
CEP41	2.2	THC2645667	2.1	RHBDL3	2.0	BCAS3	-2.0
A_32_P34064	2.2	SLC25A29	2.1	SPATA18	2.0	DNAJC10	-2.1
BG114486	2.2	RPL7L1	2.1	PLEKHA5	2.0	EFHA2	-2.1
C12orf29	2.2	CHD3	2.1	PON2	2.0	ACTG1	-2.1
ZBTB8A	2.2	RARS2	2.1	BC031320	2.0	VCL	-2.1
ASCC3	2.2	AASS	2.1	KRT18P55	2.0	COL13A1	-2.1
ATP5E	2.2	HNRNPR	2.1	GNB4	2.0	ANK1	-2.1
ENST00000378337	2.2	TUSC1	2.1	ATP5E	2.0	RTBDN	-2.1
FAM188B	2.1	A_32_P213389	2.1	SCRN1	2.0	NACC2	-2.1
PPIE	2.1	FAM43B	2.1	C6orf70	2.0	CYFIP2	-2.1
ENST00000344538	2.1	DDX19B	2.1	RXRB	2.0	PKP3	-2.1
PTGFRN	2.1	RABL3	2.1	LOC100507217	2.0	GPR89B	-2.1
TSPYL1	2.1	IFRD1	2.1	C8orf83	2.0	MST4	-2.1
RABGAP1L	2.1	HDAC2	2.1	HBP1	2.0	NBN	-2.1
CEP57L1	2.1	BP418551	2.1	MUTED	2.0	PLEKHA1	-2.1
TTC5	2.1	BQ881683	2.1	CRCP	2.0	EFR3B	-2.1

Appendix VIII Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
BC010544	-2.1	CHORDC1	-2.1	CGN	-2.2	ADAM19	-2.3
THC2497772	-2.1	C1orf54	-2.1	FZD2	-2.2	LNPEP	-2.3
PHLDA2	-2.1	ETV4	-2.1	LAMC2	-2.2	LNPEP	-2.3
C21orf91	-2.1	PDE1A	-2.1	ITGB1	-2.2	MYL12A	-2.3
ACTN1	-2.1	AKAP12	-2.2	ST3GAL5	-2.2	RGPD2	-2.3
VAC14	-2.1	A_23_P99731	-2.2	VANGL1	-2.2	CABLES1	-2.3
IGFBP6	-2.1	THC2733597	-2.2	PNPLA6	-2.2	KHK	-2.3
SLC7A5	-2.1	NUDT9	-2.2	JAG2	-2.2	STAU2	-2.4
CBX5	-2.1	PCDHA11	-2.2	BMI1	-2.2	NAT8L	-2.4
HSBP1L1	-2.1	LAMC1	-2.2	AMMECR1	-2.2	SLC39A4	-2.4
HOXC8	-2.1	EMB	-2.2	ENST00000423704	-2.3	SEC61A2	-2.4
NR4A1	-2.1	PSME2	-2.2	A_32_P172716	-2.3	TENC1	-2.4
DNMT3B	-2.1	GNPNAT1	-2.2	A_24_P400702	-2.3	INSIG2	-2.4
AK021777	-2.1	PTBP3	-2.2	A_32_P204126	-2.3	FAM111A	-2.4
FBXO2	-2.1	TNNC2	-2.2	PDE1A	-2.3	RIN1	-2.4
HS6ST1	-2.1	STAU2	-2.2	HOXC8	-2.3	DPYSL2	-2.4
DNM3	-2.1	KLF6	-2.2	CRIP2	-2.3	A_24_P15502	-2.4
SLC9A3R1	-2.1	NFKB2	-2.2	FABP5	-2.3	BMI1	-2.4
GPRASP2	-2.1	B3GNT8	-2.2	ZDHHC2	-2.3	GCC2	-2.4
AF086249	-2.1	ETHE1	-2.2	MYL12B	-2.3	DPYSL2	-2.4
A_32_P15169	-2.1	WWC2	-2.2	VCL	-2.3	SULT1A2	-2.4
EMB	-2.1	TPM1	-2.2	CXCL16	-2.3	BTN3A2	-2.4
ELMO2	-2.1	CCNB3	-2.2	INSIG2	-2.3	ETV1	-2.4
SERPINH1	-2.1	ITGB1BP2	-2.2	GNPNAT1	-2.3	IFT57	-2.4
MBNL3	-2.1	KIF26A	-2.2	CASK	-2.3	KLF6	-2.4
EML2	-2.1	SHC1	-2.2	DNM3OS	-2.3	MMP15	-2.4
PLEKHA1	-2.1	WDR1	-2.2	C10orf47	-2.3	DUSP5P	-2.4
A_24_P532730	-2.1	MT1H	-2.2	CALY	-2.3	BDP1	-2.4
CHAC1	-2.1	SYCE3	-2.2	EXOC6	-2.3	GALNT2	-2.4
C10orf35	-2.1	ATF3	-2.2	FAM111A	-2.3	ATF4	-2.4
ELK3	-2.1	CBX5	-2.2	HEYL	-2.3	FABP5	-2.4
BC010544	-2.1	THC2551769	-2.2	TMC6	-2.3	GCC2	-2.4
PIP4K2A	-2.1	KDSR	-2.2	ANKRD57	-2.3	FAM149A	-2.4
ENST00000430664	-2.1	SYNGR2	-2.2	RAPH1	-2.3	MAPKAPK3	-2.4
IL6ST	-2.1	PTGER1	-2.2	MAP3K14	-2.3	ENST00000430664	-2.4
C21orf91	-2.1	KCNG1	-2.2	BF210146	-2.3	EGR1	-2.4
A_32_P10623	-2.1	CXorf23	-2.2	GCA	-2.3	A_23_P14432	-2.4
ITGB1	-2.1	SOX7	-2.2	BDP1	-2.3	LTB	-2.4
DNAH10	-2.1	AKAP12	-2.2	A_24_P802562	-2.3	BOLA1	-2.4
CLPTM1L	-2.1	NBN	-2.2	LRRC8D	-2.3	CCR5	-2.4
TMEM191A	-2.1	CU692385	-2.2	ITM2C	-2.3	SPRY2	-2.4

Appendix VIII Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ENST00000431244	-2.4	MYADM	-2.6	PSAT1	-2.8	ASRGL1	-3.0
TMSB4X	-2.4	CORO1A	-2.6	FLNA	-2.8	TMSB4X	-3.0
SH3BGR	-2.4	CASK	-2.6	RRAS	-2.8	IFITM2	-3.0
NPHP1	-2.4	BTN3A2	-2.6	NEFH	-2.8	LAG3	-3.0
GPC6	-2.4	IFIT1	-2.6	MALT1	-2.8	HERC6	-3.0
CCR10	-2.4	MYL12B	-2.6	BC035647	-2.8	PRKG1	-3.0
KDSR	-2.4	PSME1	-2.6	C5orf32	-2.8	LARP6	-3.0
TPM1	-2.5	SIX4	-2.6	DNM3OS	-2.8	IFITM3	-3.0
FABP5	-2.5	ARVCF	-2.6	UGCG	-2.8	MANEAL	-3.0
DDIT4	-2.5	PDE1A	-2.6	KLF13	-2.8	MT1X	-3.0
TRIM53P	-2.5	CYR61	-2.6	INHBE	-2.8	CARD10	-3.0
FABP5	-2.5	SIAH2	-2.6	MT1H	-2.8	MYL2	-3.0
FYCO1	-2.5	CEACAM1	-2.6	TM7SF2	-2.8	ENST00000323496	-3.0
NKD2	-2.5	PLAUR	-2.6	SGMS1	-2.8	VAMP8	-3.0
SYNGR3	-2.5	HEY1	-2.6	PTX3	-2.8	FAM183A	-3.0
ACPL2	-2.5	OBSCN	-2.6	ATP2B1	-2.8	A_23_P216071	-3.0
HECTD2	-2.5	LOC728855	-2.6	C19orf66	-2.8	REC8	-3.0
MYO1E	-2.5	SYNGR2	-2.7	A_24_P144134	-2.8	A_32_P167592	-3.0
THC2648791	-2.5	DDC	-2.7	SLC48A1	-2.9	ZDHHC21	-3.1
ENST00000538264	-2.5	EMBP1	-2.7	SEC61A2	-2.9	SCD5	-3.1
MBD2	-2.5	A_24_P383934	-2.7	THC2657355	-2.9	BAI1	-3.1
RGS1	-2.5	RAPH1	-2.7	A_24_P530977	-2.9	CXXC5	-3.1
B2M	-2.5	PRKG1	-2.7	DACT3	-2.9	CTSK	-3.1
THC2568453	-2.5	THC2682661	-2.7	A_32_P148407	-2.9	GNG8	-3.1
PSME1	-2.5	MITF	-2.7	C12orf75	-2.9	A_32_P59475	-3.1
TRPM3	-2.5	HIST2H2AA4	-2.7	SLC48A1	-2.9	DPYSL4	-3.1
APOL2	-2.5	LOC100506123	-2.7	JAK3	-2.9	CASP7	-3.1
KCNH2	-2.5	BEND4	-2.7	A_24_P418744	-2.9	FAM20C	-3.1
BCAS4	-2.5	STX18	-2.7	RGS3	-2.9	A_24_P101742	-3.1
AHNAK	-2.5	C14orf128	-2.7	PAWR	-2.9	ASRGL1	-3.1
GPR162	-2.5	STX18	-2.7	IFI35	-2.9	LOC728875	-3.1
GDF15	-2.5	VASN	-2.7	GADD45A	-2.9	CRLF1	-3.1
CD83	-2.6	GADD45B	-2.7	A_24_P221485	-2.9	MXRA8	-3.1
GKAP1	-2.6	MAP7D2	-2.7	COL18A1	-2.9	GJC3	-3.1
BDP1	-2.6	FERMT2	-2.7	MT1X	-2.9	IL26	-3.1
RANBP17	-2.6	PLXND1	-2.7	TMSB4X	-2.9	UGCG	-3.1
SLC2A3	-2.6	FOXL2	-2.7	ENST00000451939	-2.9	HEBP1	-3.1
ARHGAP22	-2.6	PHC1	-2.7	MALAT1	-2.9	BATF3	-3.1
ASNS	-2.6	NAV1	-2.7	C1S	-3.0	SLC2A14	-3.1
PCK2	-2.6	ISYNA1	-2.8	PBX3	-3.0	NOC3L	-3.1
C12orf53	-2.6	MVP	-2.8	SHC2	-3.0	ZC3H15	-3.1

Appendix VIII Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ADCY1	-3.2	AF086154	-3.5	SIGIRR	-3.8	SQRDL	-4.3
A_32_P194704	-3.2	JDP2	-3.5	THC2675062	-3.8	ZNF704	-4.3
LIF	-3.2	IFITM3	-3.5	UPP1	-3.8	AF067801	-4.3
CYR61	-3.2	FHL2	-3.5	TBC1D12	-3.8	ENST00000507916	-4.3
CDKN1C	-3.2	GLS	-3.5	RELB	-3.9	MT1E	-4.3
PDGFRB	-3.2	RNFT2	-3.5	GRRP1	-3.9	RGS16	-4.3
MAPK11	-3.2	RGS16	-3.5	LOC100131733	-3.9	SIX1	-4.3
ENST00000415104	-3.2	CEBPA	-3.5	MIR17HG	-3.9	MIR17HG	-4.3
SH3PXD2A	-3.2	EXT2	-3.5	TRPV2	-3.9	BAIAP2L2	-4.3
TLN2	-3.2	OSR2	-3.5	A_32_P100379	-3.9	TCF15	-4.3
RTKN2	-3.2	FLJ36000	-3.6	CLEC11A	-3.9	ANK3	-4.3
RRAS	-3.2	HOXB4	-3.6	NT5C2	-3.9	RIPK2	-4.3
ABCA7	-3.2	ETS2	-3.6	SRCIN1	-3.9	THC2559002	-4.3
GAS2L3	-3.3	FAM89A	-3.6	U09850	-4.0	KREMEN2	-4.3
FJX1	-3.3	ZXDA	-3.6	THC2755690	-4.0	LPP	-4.4
ERV9-1	-3.3	LYG1	-3.6	GBP4	-4.0	KRTAP7-1	-4.4
FZD3	-3.3	A_24_P7040	-3.6	ZIC1	-4.0	WIF1	-4.4
FZD3	-3.3	CXXC5	-3.6	OSGIN2	-4.0	D4S234E	-4.4
HES4	-3.3	GDAP1	-3.6	PARD6A	-4.0	ITM2A	-4.4
PALLD	-3.3	ARG2	-3.6	ANK3	-4.0	PAQR5	-4.4
WIF1	-3.3	TPM1	-3.6	CU687617	-4.0	C5orf30	-4.4
SLCO4A1	-3.3	PDLIM5	-3.6	NAB1	-4.0	TAGLN	-4.4
ZDHHC21	-3.3	MARCKS	-3.6	ESX1	-4.1	TLN2	-4.4
PLK2	-3.3	TRIB3	-3.6	BC015977	-4.1	CAMK1D	-4.4
IFITM4P	-3.3	LOC100505894	-3.6	MT1G	-4.1	A_24_P230288	-4.4
CBLN2	-3.3	SH3D21	-3.7	TFEC	-4.1	FBLN5	-4.5
LOC100130428	-3.3	EEF1A2	-3.7	LPP	-4.1	C13orf15	-4.5
MALT1	-3.4	ZFP36L1	-3.7	ASRGL1	-4.1	PDLIM5	-4.5
CEBPA	-3.4	TCF7L1	-3.7	LPP	-4.1	MSX1	-4.5
A_24_P315256	-3.4	AMOTL2	-3.7	CCR3	-4.1	GFPT2	-4.5
BASP1	-3.4	MT1B	-3.7	MYL9	-4.1	CPNE8	-4.5
AGAP2	-3.4	S100A4	-3.7	C2CD4C	-4.1	HLA-E	-4.5
RTN4RL2	-3.4	ZNF506	-3.7	LPP	-4.1	OSGIN2	-4.5
MGAT5	-3.4	SERPINF1	-3.7	CKB	-4.1	CPNE8	-4.5
B2M	-3.4	BTN3A1	-3.7	CCDC88C	-4.1	ACTG2	-4.5
TGIF1	-3.4	TP53I11	-3.7	MYO5A	-4.1	MT1L	-4.5
RBKS	-3.4	SEMA3B	-3.7	NGEF	-4.2	MSX1	-4.6
IER3	-3.4	GADD45B	-3.7	WFIKKN1	-4.2	FBXO16	-4.6
ITPR1	-3.5	CLGN	-3.8	TBC1D12	-4.2	SIX4	-4.6
CYR61	-3.5	AK024926	-3.8	SMCR5	-4.2	ANK3	-4.6
LSR	-3.5	SSFA2	-3.8	PTRF	-4.2	C11orf88	-4.6

Appendix VIII Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SGCA	-4.6	THC2729899	-5.2	HLA-E	-6.0	PARP14	-6.9
RDH10	-4.6	SCN9A	-5.2	HLA-A	-6.0	FES	-7.0
IL15	-4.7	ENST00000485364	-5.3	CFHR3	-6.0	FGB	-7.0
RDH10	-4.7	ABCA3	-5.3	AL832534	-6.0	FGG	-7.0
NES	-4.7	A_24_P178444	-5.3	IRF9	-6.1	GRASP	-7.0
MT2A	-4.7	MAGI3	-5.3	PTRF	-6.1	BC053880	-7.1
IL17RD	-4.7	SNX16	-5.3	LTF	-6.1	HLA-B	-7.1
A_32_P78488	-4.7	THBS1	-5.3	ITGAV	-6.1	FW340012	-7.1
ZIC1	-4.8	SCN9A	-5.3	CPEB1	-6.1	FBXO15	-7.1
IFITM1	-4.8	LIN28A	-5.3	TPM1	-6.1	APC2	-7.1
NFKBIZ	-4.8	PFKP	-5.4	METRNL	-6.1	CFH	-7.2
EIF5A2	-4.8	GALNTL1	-5.4	COTL1	-6.1	FAM155B	-7.2
SOCS2	-4.8	DHX58	-5.4	RBMS3	-6.1	RBMS3	-7.2
SOCS2	-4.8	A_24_P358606	-5.4	TPM1	-6.1	FILIP1L	-7.2
RIPK2	-4.8	DBNDD2	-5.4	TLE4	-6.1	CFH	-7.3
CR749547	-4.8	SCN9A	-5.5	CNN1	-6.2	XKR6	-7.3
RASIP1	-4.9	APC2	-5.5	FZD5	-6.2	FAM198A	-7.4
DDX58	-4.9	TPM1	-5.5	HLA-DRB5	-6.2	UCP2	-7.4
TEX19	-4.9	GAB2	-5.5	BST2	-6.2	PDGFRA	-7.4
HLA-E	-4.9	FZD5	-5.6	VAV3	-6.2	COLEC11	-7.4
CLMN	-5.0	ERAP2	-5.6	FAM167A	-6.2	TYRP1	-7.4
CTSZ	-5.0	HOXB6	-5.6	MAP1B	-6.3	HLA-C	-7.4
MT2A	-5.0	USP18	-5.6	HLA-G	-6.3	HLA-B	-7.4
CACNG7	-5.0	TRIB3	-5.7	C11orf88	-6.4	ADRA2C	-7.4
TNFRSF12A	-5.0	PLAU	-5.7	ERO1LB	-6.4	COTL1	-7.5
CPA2	-5.0	ETS2	-5.8	A_32_P207789	-6.4	XAF1	-7.5
CEND1	-5.0	STAU2	-5.8	HLA-L	-6.5	RHOU	-7.6
SPOCK2	-5.0	PRKCA	-5.8	PYGM	-6.5	HLA-F	-7.6
OTX1	-5.1	ITGAV	-5.8	PDLIM5	-6.5	THC2700145	-7.6
MT2A	-5.1	MYL7	-5.9	FXYD5	-6.6	CD248	-7.6
C1QTNF6	-5.1	A_24_P401051	-5.9	GPR56	-6.6	NRIP1	-7.7
ARMC9	-5.1	AI056399	-6.0	DHRS2	-6.6	HLA-B	-7.8
MYLPF	-5.1	FCHO1	-6.0	MAB21L1	-6.6	HRK	-7.8
MGAT4A	-5.1	UNC13A	-6.0	STC2	-6.6	TLE4	-7.8
CRABP2	-5.1	RBMS3	-6.0	MAP1B	-6.7	BC038556	-7.8
DDAH1	-5.2	AK055647	-6.0	S73202	-6.7	SLC5A12	-7.8
CFH	-5.2	UBE2L6	-6.0	KLF2	-6.7	IRF1	-7.8
USP18	-5.2	ERO1LB	-6.0	FZD5	-6.7	NFE2	-7.9
TESC	-5.2	AK001808	-6.0	OASL	-6.8	CD69	-7.9
ENST00000555442	-5.2	TRIM7	-6.0	STAT1	-6.8	CAV1	-7.9
C5	-5.2	NUPR1	-6.0	COTL1	-6.9	SLC7A7	-7.9

Appendix VIII Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ZFHX2	-7.9	POC1B	-9.3	BST2	-11.5	FAM102B	-15.6
IFIT3	-8.0	FAM133A	-9.3	SRPX2	-11.6	SOCS3	-15.7
ITGA6	-8.0	DIRAS3	-9.3	A_24_P101771	-11.6	FAM171B	-15.8
IL21R	-8.0	APC2	-9.4	TMEM2	-11.7	A_32_P67303	-16.1
HLA-J	-8.0	IGFN1	-9.4	KLHDC8A	-11.8	FAM171B	-16.3
CASP1	-8.0	RCAN1	-9.5	SFTA3	-11.8	A_23_P125109	-16.3
NEAT1	-8.1	QRFPR	-9.6	NUDT11	-11.8	DIO3	-16.4
KLF7	-8.1	KIF1A	-9.6	INA	-11.9	HTR2B	-16.5
SNCG	-8.1	DPYSL5	-9.6	EYA4	-12.0	GLDC	-16.6
HLA-H	-8.2	SVIL	-9.6	AQP9	-12.1	KCNA7	-16.7
NETO2	-8.2	HTR7P1	-9.7	ZPLD1	-12.3	HCG23	-16.7
SAA2	-8.2	HLA-C	-9.7	IFI27	-12.4	ENST00000415106	-17.0
LIMCH1	-8.3	EOMES	-9.8	PPP1R1C	-12.6	TAP1	-17.1
FOXP2	-8.3	HLA-C	-9.8	VIL1	-12.8	XAF1	-17.3
STAT1	-8.3	SAA1	-9.9	DDX60	-12.8	DDX60L	-17.4
NXNL2	-8.3	NTNG1	-9.9	PLCL2	-12.8	FGF18	-17.4
BATF2	-8.4	AIG1	-10.0	COL11A1	-12.9	HOXB9	-17.4
HLA-C	-8.4	PTH2	-10.0	MFAP4	-12.9	ENST00000419364	-17.5
MORC4	-8.4	MMP3	-10.0	MMP10	-13.0	GATM	-17.6
CCR1	-8.5	RTN4RL1	-10.1	MMP1	-13.0	C4orf32	-17.7
ENKUR	-8.5	JAG1	-10.2	A_23_P421323	-13.1	LGR4	-17.9
NTF4	-8.5	PSMB9	-10.2	TES	-13.4	GJA1	-18.1
A_32_P138666	-8.5	HOXB5	-10.2	PI15	-13.4	ENST00000504916	-18.1
CFD	-8.5	ARMC9	-10.3	NRP1	-13.5	ESRRG	-18.1
CSTA	-8.5	IFI27	-10.3	PLCE1	-13.7	CAV1	-18.2
BC034319	-8.5	VMO1	-10.4	ARMC9	-13.8	ENST00000551107	-18.5
CRB1	-8.6	PAG1	-10.5	GBP3	-13.9	TCEAL5	-18.9
CD40	-8.6	COL16A1	-10.6	OCLN	-13.9	THC2677011	-18.9
ENO3	-8.6	TAGLN	-10.6	TNFRSF14	-14.0	CALCRL	-19.8
TRPM3	-8.7	CYP1B1	-10.6	NLRC5	-14.1	PCSK7	-19.9
CD47	-8.8	HTR7	-10.8	PRKCH	-14.1	HOXB6	-20.0
A_32_P106980	-8.8	MET	-10.8	SLC15A3	-14.4	C11orf75	-20.1
HLA-A	-8.9	COL6A3	-10.8	KCNA7	-14.4	SH3BP4	-20.2
HIST3H2BB	-9.0	NEO1	-10.8	RBPMS	-14.5	THC2675966	-20.3
TNNC1	-9.0	CP	-10.8	NEDD4L	-14.6	FIBIN	-20.4
TTC30A	-9.0	DHRS2	-11.1	FAM171B	-14.9	BTNL9	-20.6
EPHA10	-9.0	AF038185	-11.1	L1TD1	-15.1	AGT	-20.9
CXCR4	-9.1	NEDD4L	-11.2	FRMD7	-15.1	TES	-21.0
NP111779	-9.1	STC2	-11.4	L3MBTL4	-15.3	AK092921	-21.1
ADAMTS6	-9.2	RASGRP2	-11.5	WDR72	-15.3	GIMAP2	-21.4
KANK4	-9.2	GBP3	-11.5	PNOC	-15.3	NEDD4L	-21.6

Appendix VIII Gene Expression Changes in $A2780_{DXL\text{-}CC}$ vs. $A2780_{CC}$ (FDR=0.01, $p \leq 0.05$, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
LAMA1	-21.7	KIAA2022	-26.0	THC2676635	-39.7	A_32_P106615	-75.7
SLC16A3	-21.8	FBXL16	-26.1	IL7	-40.0	ALPK2	-77.8
TNMD	-22.0	TAC1	-26.1	NAV3	-40.3	AK129542	-82.5
PLA2G3	-22.0	COLEC12	-26.3	ZNF439	-40.6	ZFP42	-86.8
PLA2G16	-22.1	SP140	-27.1	CRISPLD1	-41.1	ZNF521	-98.3
BIRC3	-22.2	RFTN1	-27.3	ADM	-41.8	MEOX2	-104.7
RBMS1	-22.3	TRPC4	-27.7	WNT3A	-44.1	TLR3	-105.9
ONECUT1	-22.5	SLIT2	-28.6	IFNG	-45.6	TMEM47	-129.3
NUAK2	-22.7	HLA-H	-29.9	TMEM30B	-47.6	CXorf57	-130.3
SATB1	-22.7	BC028039	-30.0	BCL2	-48.9	NOX4	-159.5
TAC1	-22.7	LRRTM4	-30.4	FGF18	-49.8	MDFIC	-177.7
ARHGAP28	-22.7	LOC100192378	-33.2	THC2681889	-50.5	FLRT3	-178.2
HOXB8	-22.8	DSEL	-33.4	FAM129A	-51.3	CCR1	-195.3
XAF1	-23.1	SP110	-33.6	LAYN	-52.3	GPR158	-199.2
TCEAL3	-23.6	TBC1D8B	-33.6	FGF20	-53.8	GBP1	-204.0
TMSB15B	-23.7	DOCK3	-35.1	ARHGAP28	-54.2	GPM6A	-252.2
PYGM	-24.7	RBMS1	-35.9	GLUL	-55.3	MUM1L1	-263.7
A_23_P314024	-25.2	SDC2	-36.7	DUSP6	-70.1	EMP1	-265.6
HLA-A	-25.4	PHOX2B	-37.0	PPP1R1C	-70.4	SLC25A24	-682.6
FOLH1	-25.5	NLGN4X	-37.1	FZD8	-71.7		
PREX1	-25.7	DSEL	-39.5	ANO3	-73.0		

Appendix IX 435 Gene Expression Changes representing docetaxel resistance establishment in $A2780_{CBN\text{-}DXL}$ cell line

(FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
ATP6V0D2	35.7	MCF2L-AS1	3.0	ESPL1	2.5	APOBEC3B	2.3
SLITRK6	21.8	SHROOM2	3.0	SLC25A40	2.5	TBC1D5	2.3
MECOM	20.3	THC2699069	3.0	SIX4	2.5	B3GNT1	2.3
SULF1	18.4	ADAMTS3	3.0	POLE2	2.5	OXCT1	2.2
HAPLN1	17.1	PLK1	3.0	LOC100127983	2.5	CALM1	2.2
PRL	16.6	C20orf96	2.9	LMO7	2.5	ZFHX2	2.2
PRR16	16.0	KIAA1147	2.9	DLAT	2.4	A_32_P121674	2.2
BEX1	15.5	STYX	2.9	RCAN3	2.4	TPD52	2.2
RND3	15.3	A_24_P230009	2.9	A_32_P2303	2.4	WNK2	2.2
PLEKHG4	9.8	THRA	2.9	RPL22L1	2.4	PECR	2.2
IGFBP5	8.0	SRPX	2.9	PIF1	2.4	GPC4	2.2
NTS	7.1	LOC100505932	2.9	C1orf106	2.4	PCBD2	2.2
ARID5B	6.3	ALDH1A3	2.9	ZNF323	2.4	GLDC	2.2
DCN	5.8	C5orf39	2.9	CHEK1	2.4	SUMO3	2.2
POU4F1	5.6	STMN3	2.8	ANXA11	2.4	TRIM45	2.2
PBX1	5.5	TBC1D23	2.8	UBE2H	2.4	TMEM126A	2.2
DPYSL5	4.9	AMOT	2.8	GHR	2.4	PHF19	2.2
CDKL5	4.9	C2CD4C	2.8	DEPDC1B	2.4	MOK	2.2
SLC16A3	4.8	C19orf51	2.8	FAM198A	2.4	LRR1	2.2
CYB5A	4.7	MIS18BP1	2.8	BORA	2.4	MCM3AP-AS1	2.2
SCHIP1	4.7	COMTD1	2.8	FBXO4	2.4	RAD51AP1	2.2
CA2	4.5	HMGN5	2.8	THC2732175	2.4	ENST00000494075	2.2
FILIP1L	4.4	RAB3IP	2.8	THC2656479	2.4	KIF18A	2.2
FAM198B	4.3	TMEM65	2.7	FOXM1	2.4	PKN3	2.2
THC2770932	4.3	TMEM19	2.7	UBR7	2.4	SH2D4A	2.2
PLA2G16	4.2	TMC6	2.7	NDRG2	2.4	SALL2	2.2
CT45A1	4.1	IKBKE	2.7	C10orf76	2.4	STARD8	2.2
TNS3	4.1	OLFML3	2.7	ATL3	2.4	DISP2	2.2
BCHE	4.0	PPM1F	2.7	ZNF695	2.4	CKLF	2.2
RNF213	3.9	A_24_P178475	2.7	UCHL5	2.3	MRPL35	2.2
FBLN5	3.9	LOC100240734	2.7	C14orf93	2.3	CCDC28B	2.2
SYCP2	3.8	CAND2	2.7	RNFT2	2.3	TP53I3	2.2
GRB14	3.8	E2F7	2.7	MSI2	2.3	MFSD3	2.2
NUP210	3.6	G2E3	2.7	LMCD1	2.3	TSPAN7	2.2
MCAM	3.4	DIP2A	2.6	LOC100506054	2.3	A_32_P174385	2.2
ITPKB	3.4	CXorf57	2.6	ENST00000521696	2.3	ELL3	2.2
KIF14	3.3	THC2676635	2.6	FBXO16	2.3	PCNT	2.2
RBM43	3.3	A_24_P409440	2.6	TESC	2.3	NUF2	2.2
CDH10	3.3	OSR2	2.6	TFDP2	2.3	GRIN2C	2.1
ENST00000375678	3.3	TPMT	2.6	ARRB1	2.3	AIM1L	2.1
RASSF5	3.3	RASGRP2	2.6	LOC100131170	2.3	A_24_P178167	2.1
EEF1A2	3.2	LOC145757	2.6	SPEG	2.3	THC2517184	2.1
WNT3A	3.2	FAM120C	2.6	HIBCH	2.3	CKAP2L	2.1
HRSP12	3.1	KIF15	2.5	MFSD4	2.3	C12orf48	2.1
C1orf21	3.1	PHF15	2.5	HBQ1	2.3	SMC2	2.1
GREB1	3.1	A_32_P182135	2.5	PRDM15	2.3	A_32_P760762	2.1
LRRCC1	3.1	BOLA1	2.5	C9orf40	2.3	FAM82B	2.1
SIPA1L2	3.1	CRISPLD1	2.5	ZNF197	2.3	AK094175	2.1
		RBM20	2.5				

Appendix IX 435 Gene Expression Changes representing docetaxel resistance establishment in $A2780_{CBN\text{-}DXL}$ cell line

(FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SLC2A4RG	2.1	LOC100506965	2.0	PHF14	-2.1	DPH3	-2.2
WNT3	2.1	AGPS	2.0	PCMT1	-2.1	MME	-2.2
ATXN3	2.1	UBR5	2.0	ROR2	-2.1	LRRTM4	-2.2
HIRIP3	2.1	BPTF	2.0	IFI27L2	-2.1	TULP4	-2.2
SLC39A4	2.1	GALNTL1	2.0	KIAA1919	-2.1	LOC80054	-2.2
RBBP5	2.1	ZNF273	2.0	DDX19B	-2.1	ASS1	-2.2
SMYD2	2.1	DLEU1	2.0	ST6GALNAC6	-2.1	A_24_P306814	-2.3
PCDH17	2.1	DSCC1	2.0	BI256572	-2.1	USP14	-2.3
FKBP3	2.1	ENST00000523354	2.0	PDCD2	-2.1	IGF1R	-2.3
PDE9A	2.1	PLBD1	2.0	HES4	-2.1	SFT2D1	-2.3
WDR76	2.1	MRE11A	2.0	C13orf15	-2.1	SLC7A11	-2.3
AZI1	2.1	GPD2	2.0	C6orf120	-2.1	TRAPPC6A	-2.3
GNG2	2.1	ZWINT	2.0	BC049371	-2.1	BM683477	-2.3
NCAPH	2.1	CTSL2	2.0	FTL	-2.1	LOC647979	-2.3
CENPP	2.1	LRBA	2.0	CRADD	-2.1	SAP18	-2.3
CCDC125	2.1	TMPO	2.0	CYBRD1	-2.1	A_24_P660797	-2.3
ARL6IP5	2.1	HSPB1	2.0	NR2F1	-2.1	XBP1	-2.3
LOC100505771	2.1	LOC338799	2.0	RBCK1	-2.1	HOXB5	-2.3
C14orf33	2.1	ZC4H2	2.0	TCF15	-2.1	HLA-B	-2.3
MAPK12	2.1	RACGAP1	2.0	A_32_P78488	-2.1	BMP7	-2.3
LSM3	2.1	COLEC12	2.0	FAM106A	-2.1	PGM3	-2.3
MTA3	2.1	NUCKS1	2.0	ME1	-2.1	ASPH	-2.3
CTBP1	2.1	CACNB3	2.0	LOC728739	-2.1	KPNA5	-2.4
WDR90	2.1	GRAMD1C	2.0	THC2660636	-2.1	A_24_P33055	-2.4
A_24_P281175	2.1	CENPA	2.0	KLHDC7B	-2.1	ATP1B1	-2.4
TOP2A	2.1	RAB8B	2.0	MSH3	-2.1	SSH3	-2.4
FANCD2	2.1	TRMT1L	2.0	A_24_P358606	-2.1	SLC22A18	-2.4
RXRA	2.1	CCR10	2.0	MBL2	-2.1	NUS1	-2.4
CLEC2D	2.1	CCDC138	2.0	A_24_P692600	-2.1	C1S	-2.4
CKMT1A	2.1	GNB4	2.0	RGS1	-2.1	CNKSR3	-2.4
ANG	2.1	WDR34	2.0	ACADVL	-2.1	COL3A1	-2.4
KLHDC8B	2.1	PRMT2	2.0	MTHFD1L	-2.1	GJA1	-2.4
FANCG	2.1	THC2783023	-2.0	NFE2L1	-2.1	RSPH3	-2.4
CCDC88A	2.1	GOT1	-2.0	BC073815	-2.1	NUPL1	-2.4
PSMB10	2.1	COQ10B	-2.0	TPRG1L	-2.2	IGF2R	-2.4
MYCBP	2.1	UFM1	-2.0	S73202	-2.2	NHSL1	-2.4
C18orf54	2.1	PIGM	-2.0	AL832534	-2.2	SEC63	-2.4
HCFC2	2.1	BE780682	-2.0	ZNRF1	-2.2	HTR7	-2.5
A_24_P92823	2.1	HIST1H2BL	-2.0	KRCC1	-2.2	A_32_P128399	-2.5
TRIM66	2.1	BC000206	-2.0	C6orf192	-2.2	EFCAB1	-2.5
INCENP	2.1	HIST1H2BH	-2.0	PRPH	-2.2	SEZ6L2	-2.5
A_32_P4608	2.1	C6orf70	-2.0	ZNF295	-2.2	AK130366	-2.5
CEP250	2.1	RAB2A	-2.0	GBE1	-2.2	TCN2	-2.5
DKK3	2.0	C18orf8	-2.0	BC041955	-2.2	AF038185	-2.5
LRRC40	2.0	A_32_P123589	-2.0	A_24_P178444	-2.2	STXBP1	-2.5
ARHGEF16	2.0	HSPA4	-2.0	ZBTB46	-2.2	GPR56	-2.6
NUDT1	2.0	A_24_P367100	-2.0	TAGLN	-2.2	AK094629	-2.7
CCDC88B	2.0	HIST1H2BF	-2.1	LOC100133920	-2.2	CTGF	-2.7
SEC22C	2.0			A_24_P871726	-2.2	PABPC4L	-2.7

Appendix IX 435 Gene Expression Changes representing docetaxel resistance establishment in $A2780_{CBN\text{-}DXL}$ cell line

(FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
MYO15A	-2.7						
DLG2	-2.7						
ENOX1	-2.8						
PIK3C3	-2.8						
SNX9	-2.8						
ARNT2	-2.9						
UNC5B	-2.9						
OSTM1	-3.0						
CD24	-3.0						
FXYD1	-3.1						
S100A1	-3.1						
AKAP12	-3.2						
SGCA	-3.2						
CD164	-3.2						
LIPA	-3.3						
GADD45A	-3.3						
F10	-3.3						
SH3GL3	-3.4						
HOXB13	-3.4						
LHX2	-3.5						
ACAT2	-3.5						
A_32_P145159	-3.5						
RAB7B	-3.6						
FNDC1	-3.7						
TMEM181	-3.8						
LOC100131053	-3.9						
THC2675966	-4.0						
THC2675062	-4.0						
SCN7A	-4.2						
FOXD2	-4.3						
THC2644672	-4.5						
ALDH1A1	-4.6						
ATF5	-5.1						
DMD	-5.2						
FGG	-5.3						
MMP3	-6.2						
BC005081	-7.4						
EFNA5	-9.3						
QKI	-9.8						
ANK3	-9.9						
A2M	-10.4						
CFHR3	-11.6						
AKR1C1	-11.8						
CFH	-14.0						
CR749547	-14.9						

Appendix X 1319 Gene Expression Changes representing carboplatin resistance establishment in $A2780_{DXL\text{-}CBN}$ cell line

(FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
SLC25A24	793	LOC100505971	27.8	PSMB9	12.5	RCAN1	8.0
PITX2	220	PREX1	26.0	TNFRSF14	12.3	ADRA2C	7.9
ZFP42	179	AGT	26.0	APOL6	12.1	GAB2	7.9
GPR158	172	SP110	25.8	IFI27	12.0	KCNA7	7.9
ZNF521	137	SP140	24.9	DUSP27	11.6	AK092921	7.8
LRRTM4	127	DOCK3	24.6	HCG23	11.6	INA	7.8
ALPK2	107	TCEAL6	24.4	TLR3	11.4	CLGN	7.7
GBP1	101	C11orf75	24.2	RASGRP2	11.3	STXBP6	7.7
TMEM30B	96.2	PLA2G3	23.5	L3MBTL4	11.2	FAM129A	7.7
CRISPLD1	96.0	CLDN17	23.4	GBP4	11.2	DHRS2	7.6
TMEM47	93.0	ONECUT1	22.9	WDR72	11.2	ELF3	7.6
NOX4	91.3	BTNL9	22.2	CRISP1	11.1	PLAU	7.6
FOLH1B	89.0	SAA1	22.2	CASP1	11.0	LRFN5	7.5
CXorf57	86.0	TRPS1	20.8	PLCL2	11.0	FJX1	7.4
KITLG	85.9	SOCS3	20.7	CNDP1	10.9	NES	7.4
TNFRSF19	59.7	ENST00000551107	19.9	PDGFA	10.9	SYTL4	7.4
THC2681889	57.9	NEDD4L	19.4	ADM	10.8	IL1RAPL2	7.4
FRY	55.2	ARHGAP28	19.2	ENST00000504916	10.7	MAT1A	7.3
MUC15	53.2	FIBIN	18.7	MID2	10.6	LCP1	7.2
SUN3	51.7	TAC1	18.7	VMO1	10.6	FAM198A	7.2
RNF128	50.0	TNMD	18.6	VLDLR	10.5	THBS1	7.2
GSG1	49.4	DIO3	18.3	FOXA1	10.5	AGAP2	7.2
AGMO	47.1	ALCAM	18.2	IFIT3	10.3	PLOD2	7.1
GRIK1	46.0	NETO1	18.2	PTH2	10.2	GATM	7.0
FOLH1	45.5	OTOL1	17.8	UBA7	10.1	LOC283454	7.0
ZNF439	44.5	POC1B	17.4	CD40	10.0	CCR1	7.0
GLUL	44.2	PI15	17.3	ARPP21	10.0	DDX60L	6.9
PCDH15	43.0	IL21R	17.1	FAM102B	9.9	IL17RD	6.9
SH3BP4	42.9	GIMAP2	17.1	RTN4RL1	9.8	CNRIP1	6.9
COLEC12	42.6	PLXDC2	16.9	AI056399	9.8	D4S234E	6.9
WNT3A	42.6	POSTN	16.0	THC2700145	9.8	FAM155B	6.9
LZTS1	41.5	FLJ35024	16.0	TNNC1	9.6	VAMP8	6.8
SLIT2	41.2	SLC16A3	15.7	MET	9.3	EGR1	6.7
NAV3	39.0	BCL6	15.5	EMP1	9.3	TMEM158	6.7
TCEAL5	39.0	FCHO1	15.5	LGR4	9.2	TGIF1	6.6
MEOX2	37.5	NEO1	15.3	FAM171B	9.1	SCD5	6.5
TCEAL3	37.2	C4orf32	15.2	EPHA10	9.1	ENO3	6.5
FGF20	37.0	CD248	15.1	TAP1	9.0	APC2	6.4
SPG20	34.3	GLDC	14.9	SNCG	8.8	FZD5	6.4
DA727827	34.1	SLC15A3	14.8	RBMS1	8.7	TRIML2	6.4
HOXB8	33.7	PCSK7	14.4	MDFIC	8.6	PAG1	6.4
PRKCH	33.2	TRPC4	14.3	METRNL	8.5	TMEM150C	6.4
IFNG	32.8	SAA2	13.7	RGS16	8.4	PNOC	6.3
SDC2	32.0	ITGA6	13.4	FAM89A	8.4	TCF15	6.2
LOXL1	31.4	PCDH19	13.0	COL6A3	8.3	HIF3A	6.2
DSEL	31.3	ZNF585A	13.0	PNMA2	8.3	IRF9	6.2
ADAMTS1	29.4	TMEM2	12.9	OCLN	8.3	EFNA5	6.1
HSPA1A	28.1	BATF2	12.7	LOC100506674	8.2	CAV1	6.1

Appendix X 1319 Gene Expression Changes representing carboplatin resistance establishment in $A2780_{DXL\text{-}CBN}$ cell line

(FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
PTRF	6.1	E01979	4.8	EHBP1L1	3.9	BRF1	3.3
STAT1	5.9	C11orf96	4.7	LOC100131733	3.9	NR4A1	3.3
MYEF2	5.9	TBC1D12	4.7	THC2637858	3.8	EPB41L5	3.3
CACNG7	5.9	ISG15	4.7	FW340012	3.8	AK026418	3.3
OSGIN2	5.8	DBNDD2	4.6	KCNG1	3.8	CENPA	3.3
SPOCK2	5.8	FIGN	4.6	ENST00000415104	3.8	USP18	3.3
THC2755690	5.7	RDH10	4.6	CGN	3.8	GPR107	3.3
FHL2	5.7	THC2651023	4.6	SLC2A3	3.8	NUPR1	3.2
C1QTNF6	5.7	UCP2	4.5	SLC39A4	3.7	BICD1	3.2
ENST00000485364	5.6	PYGM	4.5	MALT1	3.7	C12orf53	3.2
AMOTL2	5.5	CORO1A	4.4	C1orf187	3.7	LOC100505894	3.2
TMCC3	5.5	AK055647	4.4	BC034319	3.7	ACOT7	3.2
HTR7	5.5	CCRL2	4.4	CPEB1	3.7	MAPK11	3.2
ERC2	5.5	ITGAV	4.3	HLA-G	3.6	PIK3CA	3.2
H19	5.5	PKP3	4.3	BOLA1	3.6	CCR10	3.2
GNB5	5.4	LOC728855	4.3	BAI1	3.6	FAM57B	3.2
EPHA7	5.4	EFR3B	4.3	MAP7D2	3.6	THC2707492	3.2
GALNTL1	5.4	HLA-J	4.3	LRRC8C	3.6	RAPH1	3.2
TSPAN5	5.4	SNX16	4.2	COTL1	3.6	FZD2	3.2
THC2675062	5.4	HEBP1	4.2	CPNE8	3.6	SIX1	3.2
ZFP36L1	5.3	ZNF704	4.2	MEIS3	3.5	HLA-B	3.2
SH3D21	5.3	PLAUR	4.2	TLN2	3.5	LOC84989	3.2
TTC30A	5.3	ERV9-1	4.2	H1F0	3.5	NP111779	3.2
CD47	5.3	C11orf88	4.2	EIF5A2	3.5	NEURL1B	3.2
CARD10	5.3	MEF2C	4.1	RNFT2	3.5	ENST00000507916	3.2
IGFN1	5.3	LOC728875	4.1	NUDT10	3.5	LOC100288675	3.2
CLEC11A	5.2	PLK5	4.1	MYL12B	3.5	FSD1	3.1
EGFR	5.2	BC028022	4.1	ARG2	3.5	B3GNT2	3.1
KREMEN2	5.2	RTN4R	4.1	IQCD	3.5	MT1L	3.1
TRIM64	5.1	ETV4	4.1	ERAP2	3.5	SAMD14	3.1
ARHGEF16	5.1	ACPL2	4.1	MCAM	3.4	PSME2	3.1
ENST00000538264	5.1	ZNF506	4.1	SYNGR3	3.4	MYADM	3.1
CRABP2	5.0	SORT1	4.1	TRIB1	3.4	WFIKKN1	3.1
DACT3	5.0	KIAA1274	4.0	EPN3	3.4	KHDC1	3.1
JPH3	5.0	TEX19	4.0	CRADD	3.4	RARRES3	3.1
IGSF9	4.9	IL20RB	4.0	HLA-H	3.4	ZSCAN2	3.1
ST8SIA1	4.9	TAGLN	4.0	ARVCF	3.4	S73202	3.1
HEYL	4.9	ENST00000539135	4.0	VASN	3.4	RANBP17	3.1
UNC13A	4.9	OTX1	4.0	LRRN3	3.4	UBE2L6	3.1
GAS2L3	4.9	RPH3AL	4.0	KRTAP7-1	3.4	GPR20	3.0
PARP9	4.9	PARP14	4.0	RIPK2	3.4	MT1G	3.0
C1orf198	4.9	FUT1	4.0	FAM176B	3.4	HLA-F	3.0
C2CD4C	4.9	HIST1H2AB	4.0	RTN4RL2	3.3	NOS2	3.0
EPS8L1	4.9	SLC48A1	3.9	CFD	3.3	C21orf30	3.0
MAGI3	4.8	ATP2B1	3.9	SRCIN1	3.3	MT1H	3.0
BC038432	4.8	FXYD5	3.9	RASL11B	3.3	CU687617	3.0
IRF1	4.8	GPC6	3.9	MT2A	3.3	OSR2	3.0
ZNF507	4.8	RAB3IP	3.9	ADNP2	3.3	IER5L	3.0

Appendix X 1319 Gene Expression Changes representing carboplatin resistance establishment in $A2780_{DXL\text{-}CBN}$ cell line

(FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
KCNJ4	3.0	PAWR	2.8	RELL1	2.6	RASL10A	2.4
MT1X	3.0	COLEC11	2.8	RPGR	2.6	PAOX	2.4
NGEF	3.0	AL832534	2.8	CITED4	2.6	CASP7	2.4
BC010544	3.0	VEGFB	2.8	KHK	2.6	NAT6	2.4
HLA-C	2.9	B2M	2.8	FHOD1	2.6	TSPAN6	2.4
HLA-DPA1	2.9	FERMT2	2.7	NUDT8	2.6	HIST1H2AE	2.4
ID4	2.9	DYNC2H1	2.7	USP12	2.6	SMA5	2.4
PARD3	2.9	LOC100507507	2.7	PLEKHO1	2.6	WWTR1	2.4
MIR17HG	2.9	DDT	2.7	SLC2A6	2.6	ENST00000375678	2.4
BCL2L12	2.9	REC8	2.7	C16orf48	2.6	UGCG	2.4
SLC35G1	2.9	ELL3	2.7	AA158952	2.6	PDLIM2	2.4
COL1A1	2.9	BU602485	2.7	FAM123B	2.6	GADD45B	2.4
NPHP1	2.9	BM928667	2.7	FLJ36000	2.6	TSPAN14	2.4
PTBP3	2.9	TMEM123	2.7	LRRC32	2.6	GMFG	2.4
MNAT1	2.9	SH3PXD2B	2.7	PLEKHF1	2.5	CCDC88C	2.4
AF086154	2.9	C19orf28	2.7	ARID3A	2.5	LGALSL	2.4
TNFRSF12A	2.9	ELK3	2.7	SOCS2	2.5	SLC44A1	2.4
INSIG2	2.9	KLRG2	2.7	PBX3	2.5	BTN3A2	2.4
ZC3H15	2.9	SLC25A21	2.7	GPRIN1	2.5	TBC1D9	2.4
FADS2	2.9	CXorf61	2.7	TIGD2	2.5	LIX1L	2.4
MAPK12	2.9	KDSR	2.7	CUL5	2.5	HS1BP3	2.4
TRIM49	2.9	SCAMP5	2.7	CFH	2.5	HSPB11	2.4
BEND4	2.9	CXXC5	2.7	PRKD2	2.5	PEAK1	2.4
CKB	2.9	CRIP2	2.7	RASSF4	2.5	ST6GAL1	2.4
PNPLA6	2.9	C12orf62	2.7	WDR62	2.5	TPM1	2.4
ZFP36	2.9	GFPT2	2.7	FAM46B	2.5	C19orf66	2.4
SIGIRR	2.9	NCS1	2.7	ISYNA1	2.5	ELMO2	2.4
KIRREL	2.8	RELL2	2.7	HLA-A	2.5	NRTN	2.4
LOC344967	2.8	NANOS1	2.7	CASK	2.5	ANK3	2.4
MPDZ	2.8	PLEKHG2	2.7	ZDHHC2	2.5	THC2526765	2.4
C5orf4	2.8	KAZN	2.7	ABR	2.5	S1PR2	2.4
EFNA4	2.8	KLF6	2.7	PSMB10	2.5	C1orf96	2.4
BST2	2.8	SRGAP2	2.6	LOC100287177	2.5	PEX2	2.3
ENST00000535363	2.8	MYLPF	2.6	RGPD2	2.5	CNN1	2.3
DTX3L	2.8	MORC4	2.6	HLA-E	2.5	FZR1	2.3
CKM	2.8	RIN1	2.6	KIF1A	2.5	NLGN1	2.3
MDM1	2.8	THC2689241	2.6	SH2D4A	2.5	ENST00000451939	2.3
ABCA3	2.8	LOC344595	2.6	JUP	2.5	HHEX	2.3
EPDR1	2.8	AA812298	2.6	AGGF1	2.5	FUT8	2.3
ENST00000442130	2.8	IFT57	2.6	MYOF	2.5	CCDC40	2.3
MAPKAPK3	2.8	ZFP106	2.6	GRTP1	2.5	TIPARP	2.3
ANGPTL4	2.8	COMTD1	2.6	WWC2	2.5	MITF	2.3
IGDCC3	2.8	CUBN	2.6	ACYP2	2.5	IFITM1	2.3
SGCA	2.8	MT1B	2.6	PDE4D	2.5	IFITM2	2.3
KCNH2	2.8	MYO19	2.6	ARHGAP44	2.5	AARSD1	2.3
BI832578	2.8	KLHL5	2.6	DOCK1	2.5	IMPA1	2.3
NT5C2	2.8	CARHSP1	2.6	RASGEF1A	2.4	LOC400027	2.3
FZD3	2.8	KIF26A	2.6	NOC3L	2.4	THC2657931	2.3

Appendix X 1319 Gene Expression Changes representing carboplatin resistance establishment in $A2780_{DXL\text{-}CBN}$ cell line

(FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
RAP2C	2.3	C14orf119	2.2	SLC9A6	2.1	CPSF3	2.0
CU690915	2.3	BG327427	2.2	IER2	2.1	RNF26	2.0
C16orf93	2.3	SHISA5	2.2	SREBF1	2.1	CYBRD1	2.0
IKZF4	2.3	CACYBP	2.2	AP3B1	2.1	G2E3	2.0
KLF11	2.3	PLCB3	2.2	SEC61A2	2.1	TMSB15A	2.0
CCR5	2.3	APOL2	2.2	SPSB3	2.1	DDX52	2.0
SOAT1	2.3	CDK1	2.2	ZXDA	2.1	CDK2AP2	2.0
KIAA1671	2.3	GNPNAT1	2.2	HOXC8	2.1	CHST7	2.0
FAM100A	2.3	PELI3	2.2	MMP15	2.1	TMEM126B	2.0
GCC2	2.3	GBE1	2.2	DOK4	2.1	PROCA1	2.0
ZNF780B	2.3	RASSF2	2.2	APOOL	2.1	SAC3D1	2.0
BCL3	2.3	LOC389634	2.2	LMNB1	2.1	SORD	2.0
POLE4	2.3	TTC25	2.2	HOXB3	2.1	FOXE1	2.0
PPP1R13L	2.3	ZNF395	2.2	ADAM19	2.1	VPS29	2.0
C18orf34	2.3	ZNF385A	2.2	OBSCN	2.1	UBTD1	2.0
SSSCA1	2.3	TK1	2.2	BCL2A1	2.1	LATS2	2.0
SDC4	2.3	STX10	2.2	GINS1	2.1	MYO5A	2.0
CHMP3	2.3	ITPR1	2.2	C10orf57	2.1	ILK	2.0
PPP2R1B	2.3	MYC	2.2	ABI2	2.1	WDR34	2.0
RALGAPA2	2.3	HDAC7	2.2	KRAS	2.1	GRAMD1A	2.0
KLF2	2.3	TCF7	2.1	SHC1	2.1	BDP1	2.0
ACOT9	2.2	VPS13A	2.1	HES4	2.1	YAF2	2.0
LNPEP	2.2	CCNE1	2.1	ASCC1	2.1	NPL	2.0
LRRC42	2.2	COMMD3	2.1	MED11	2.1	ENSA	2.0
C21orf90	2.2	RASSF3	2.1	GPR162	2.1	APEH	2.0
HAS3	2.2	RRP1B	2.1	ZMYM6NB	2.1	ZNF217	2.0
USP6NL	2.2	ZNF695	2.1	TYRO3	2.1	ALAD	2.0
IER3	2.2	GPC1	2.1	RAI14	2.1	MSL3P1	2.0
FAM107B	2.2	PLEKHJ1	2.1	JDP2	2.1	TMEM102	2.0
ENST00000430664	2.2	TUBB6	2.1	COMMD4	2.1	C11orf82	2.0
BC013798	2.2	KDM3A	2.1	CABLES1	2.1	C10orf47	2.0
BMI1	2.2	KCTD17	2.1	B3GNT1	2.1	LOC442421	2.0
NSMCE4A	2.2	ICAM3	2.1	CKS2	2.1	ING1	2.0
THC2645562	2.2	ACVR1	2.1	FABP5	2.1	MRPL52	2.0
S100A4	2.2	CBX5	2.1	C21orf91	2.1	IFITM3	2.0
C1S	2.2	RTEL1	2.1	C8orf58	2.1	CDH18	2.0
FLJ37453	2.2	XRCC4	2.1	INF2	2.1	P2RY2	2.0
TMEM69	2.2	HIST1H2AM	2.1	DIEXF	2.1	XM_002343200	2.0
PLA2G16	2.2	ARID3B	2.1	C12orf76	2.1	ASRGL1	2.0
EFHA2	2.2	POLD1	2.1	DOCK7	2.1	AF354444	-2.0
TESC	2.2	TPM3	2.1	DHRS11	2.1	RBAK	-2.0
RBFA	2.2	FAM20C	2.1	GALE	2.0	EEF1A1	-2.0
LOC440292	2.2	TRIB3	2.1	HSD17B1	2.0	GATC	-2.0
MESDC1	2.2	DHFRL1	2.1	PLK1	2.0	BTN2A1	-2.0
H2AFJ	2.2	IFITM4P	2.1	HPS3	2.0	GSTM4	-2.0
PML	2.2	B9D1	2.1	NCAPD2	2.0	ENST00000378337	-2.0
SDF2L1	2.2	TSPAN4	2.1	H2AFZ	2.0	PDCD2	-2.0
NUDT14	2.2	TBCD	2.1	C16orf57	2.0	BC011779	-2.0

Appendix X 1319 Gene Expression Changes representing carboplatin resistance establishment in $A2780_{DXL\text{-}CBN}$ cell line

(FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
THC2526647	-2.0	C7orf49	-2.1	HBP1	-2.2	LOC100132832	-2.4
OSTM1	-2.0	BAG1	-2.1	NGRN	-2.2	KIAA1370	-2.4
LOC100499177	-2.0	SETD1B	-2.1	ZNF764	-2.2	FBXL18	-2.4
SCN4B	-2.0	C2orf28	-2.1	DTNBP1	-2.2	TMEM38B	-2.4
AK057088	-2.0	COX1	-2.1	RABGEF1	-2.2	THC2610657	-2.4
HIST1H2BB	-2.0	GPC2	-2.1	HSPB1	-2.2	RNF146	-2.4
CUL1	-2.0	RBM5	-2.1	XIST	-2.2	NID2	-2.4
QRSL1	-2.1	HPX-2	-2.1	AK127081	-2.2	TET2	-2.4
KLF9	-2.1	ASF1A	-2.1	AK127572	-2.3	ISY1	-2.4
GPAM	-2.1	CCDC132	-2.1	RIC3	-2.3	RNF34	-2.4
SRP19	-2.1	MTHFD1L	-2.1	PHF10	-2.3	AL833005	-2.4
STK19	-2.1	CD9	-2.1	AW964144	-2.3	MGC21881	-2.4
MAP3K4	-2.1	SLC35F2	-2.1	C7orf31	-2.3	TMEM181	-2.4
PPIA	-2.1	THC2693923	-2.1	RING1	-2.3	IFNGR1	-2.4
CBWD5	-2.1	SLC4A3	-2.1	PIGS	-2.3	ACOT13	-2.4
SLC39A7	-2.1	ZNF519	-2.1	GPR135	-2.3	TMEM106B	-2.4
LOC100510011	-2.1	ZNF140	-2.1	PGAP1	-2.3	AY090769	-2.4
MTUS1	-2.1	MRPL32	-2.1	EPB41L2	-2.3	NDUFB4	-2.4
PEX12	-2.1	AK056630	-2.2	CLK1	-2.3	IFI27L1	-2.4
RIMS2	-2.1	MEPCE	-2.2	BRP44L	-2.3	SSR1	-2.4
RBM25	-2.1	ETNK2	-2.2	LOC100505794	-2.3	REPS1	-2.4
PHF2	-2.1	AY033611	-2.2	THC2701422	-2.3	FAM3C	-2.4
AK026168	-2.1	ZNF322	-2.2	SLC35B2	-2.3	SERPINB6	-2.4
C1orf162	-2.1	RPF2	-2.2	FKBP7	-2.3	BAIAP2L1	-2.5
ZNF282	-2.1	TNPO3	-2.2	SHPRH	-2.3	WTAP	-2.5
LOC400099	-2.1	SLC39A10	-2.2	LOC440356	-2.3	HIST1H2BH	-2.5
CD63	-2.1	POPDC3	-2.2	AKIRIN2	-2.3	ZBTB9	-2.5
PRPF39	-2.1	ND6	-2.2	VTA1	-2.3	ZFAND2A	-2.5
ARF5	-2.1	C14orf149	-2.2	LTV1	-2.3	WBSCR16	-2.5
CDC42BPG	-2.1	HIST1H2BO	-2.2	MRS2	-2.3	ASCC3	-2.5
WRNIP1	-2.1	TCF7L2	-2.2	CCDC80	-2.3	CEP41	-2.5
HDAC9	-2.1	FUCA2	-2.2	CHN1	-2.3	RHBDD2	-2.5
LINC00174	-2.1	FAM200A	-2.2	WBP1	-2.3	AHCY	-2.5
ANKRD18A	-2.1	ZNF498	-2.2	THC2554861	-2.3	P4HA2	-2.5
SYTL1	-2.1	FASTK	-2.2	LOC730102	-2.3	PMS2L2	-2.5
ENST00000439904	-2.1	QPRT	-2.2	THC2554943	-2.3	FAM50B	-2.5
PRKY	-2.1	PPP1R12A	-2.2	ND1	-2.3	RAB24	-2.5
ASPH	-2.1	BC031320	-2.2	RBBP6	-2.3	ECHDC2	-2.5
FV159898	-2.1	ARHGAP17	-2.2	AGAP3	-2.3	SCAND3	-2.5
NUDCD3	-2.1	SAP30	-2.2	C9orf125	-2.3	TBCC	-2.5
MOSPD1	-2.1	ZNF184	-2.2	ZUFSP	-2.3	METTL9	-2.5
MIAT	-2.1	PDIA2	-2.2	CDHR3	-2.3	ING3	-2.5
INSIG1	-2.1	SNX13	-2.2	ZBTB24	-2.4	PMS2	-2.5
TYW1	-2.1	SEC63	-2.2	LOC100507217	-2.4	NQO1	-2.5
ZBED1	-2.1	SRI	-2.2	YKT6	-2.4	LEMD2	-2.5
C10orf118	-2.1	KIF7	-2.2	SLCO5A1	-2.4	HGD	-2.5
C6orf203	-2.1	DHRS7	-2.2	ABLIM1	-2.4	LOC100506462	-2.5
ZNF721	-2.1	BAZ1B	-2.2	DSE	-2.4	TSPYL1	-2.5

Appendix X 1319 Gene Expression Changes representing carboplatin resistance establishment in $A2780_{DXL\text{-}CBN}$ cell line

(FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
GALNT6	-2.5	TMEM8B	-2.8	CD226	-3.5	ASPRV1	-4.6
PRKRIP1	-2.5	PEX1	-2.8	LOC729852	-3.5	AK124097	-4.6
ARID5B	-2.5	CUL7	-2.8	LOC100131053	-3.5	CD247	-4.6
PON2	-2.6	RXRB	-2.8	C20orf177	-3.5	STOX2	-4.7
HIST1H2BL	-2.6	C6orf168	-2.8	FSTL1	-3.5	BC037328	-4.7
EMILIN3	-2.6	TMX4	-2.8	MIOS	-3.5	CSRP2	-4.7
SOCS6	-2.6	SSR4P1	-2.8	ENST00000439362	-3.5	ADAMTS19	-4.9
THC2610134	-2.6	SYNM	-2.9	RTDR1	-3.5	BTG1	-4.9
STON1	-2.6	MDH2	-2.9	BX118285	-3.5	ENST00000479981	-4.9
GET4	-2.6	ACTR3B	-2.9	BOC	-3.6	SULT2A1	-4.9
THC2565422	-2.6	FAM160B1	-2.9	ZNF441	-3.6	EPHA3	-4.9
STEAP1	-2.6	C6orf225	-2.9	EPM2AIP1	-3.6	AGPHD1	-5.0
NEK9	-2.6	LOC283663	-2.9	SLC3A1	-3.6	SESN1	-5.1
SLMO2	-2.6	LOC220906	-2.9	CU675788	-3.6	FST	-5.1
BBS5	-2.6	RPL7L1	-2.9	ZNF862	-3.6	ELOVL4	-5.1
ZC3H6	-2.6	C6orf70	-2.9	ZDHHC8P1	-3.6	DLK1	-5.2
C15orf62	-2.6	L07392	-3.0	C6orf89	-3.6	LOC100505938	-5.2
FBN1	-2.6	GUSBP4	-3.0	ENST00000416395	-3.6	FZD1	-5.2
RGL1	-2.6	HDDC2	-3.0	ENST00000456460	-3.6	CCDC3	-5.2
NMNAT1	-2.6	AK130366	-3.0	BHLHE41	-3.7	CNTNAP2	-5.2
FKBP1B	-2.6	DCLK1	-3.0	SLC12A2	-3.7	AI698357	-5.3
LINGO2	-2.6	MTMR11	-3.0	OLFM3	-3.7	ISOC1	-5.3
DLX6	-2.7	TLE2	-3.0	ZNF462	-3.8	AK021570	-5.4
MBNL2	-2.7	AKAP9	-3.0	MAP2K6	-3.8	PRKAR2B	-5.4
TCP1	-2.7	ITPKB	-3.1	C1orf53	-3.9	WNT5B	-5.4
ZNF3	-2.7	LRRC39	-3.1	HEBP2	-3.9	MGC16121	-5.4
GTF2I	-2.7	RBAK-LOC389458	-3.1	MIR1245A	-3.9	SLC27A6	-5.5
UBE2E1	-2.7	ZSCAN21	-3.1	THC2704459	-3.9	MYCBPAP	-5.5
ARL17A	-2.7	DMKN	-3.1	THC2785860	-3.9	OXR1	-5.6
CASD1	-2.7	RIOK1	-3.1	KLHL14	-3.9	COL2A1	-5.7
C6orf26	-2.7	ATP11C	-3.1	ENST00000433980	-4.0	RGS11	-5.9
LOC100131564	-2.7	PRSS16	-3.1	BI836406	-4.0	FABP7	-6.1
DLEU2	-2.7	RHOBTB3	-3.2	UBR3	-4.0	B3GNT5	-6.2
ST7	-2.7	C6orf204	-3.2	MCOLN2	-4.0	LRRC17	-6.3
NUS1	-2.7	THC2713242	-3.2	TMEM35	-4.0	C4orf34	-6.3
ULK2	-2.7	TMEM117	-3.2	DTX3	-4.1	BAALC	-6.4
MMP11	-2.7	ENST00000435913	-3.2	TTC39A	-4.1	PBX1	-6.4
PEX6	-2.7	ZNF76	-3.2	FAM82A1	-4.1	SERPINB1	-6.6
PKIG	-2.7	CYCS	-3.3	AK7	-4.1	CA13	-6.6
PDCD7	-2.7	PURB	-3.3	B4GALT1	-4.1	ENST00000521369	-6.6
HCFC2	-2.7	THC2744399	-3.3	CITED1	-4.2	NEGR1	-6.7
GOSR1	-2.7	IFRD1	-3.3	DYNLT3	-4.2	CAST	-6.8
CTH	-2.7	ISL1	-3.3	BC016022	-4.2	SNX7	-7.1
TAOK3	-2.7	SIRT1	-3.4	DSCR6	-4.3	RTTN	-7.1
ODZ3	-2.7	URGCP	-3.4	TAC3	-4.3	GPC3	-7.1
PTEN	-2.7	ENST00000422603	-3.4	FAM169A	-4.4	SYCP3	-7.1
KIAA1586	-2.8	FAM168A	-3.4	PLCH1	-4.4	FOXN4	-7.2
SLC22A5	-2.8			PAPSS2	-4.4	BEGAIN	-7.2

Appendix X 1319 Gene Expression Changes representing carboplatin resistance establishment in $A2780_{DXL\text{-}CBN}$ cell line

(FDR=0.01, p≤0.05, variation ≥2-fold)

Gene name	Fold change	Gene name	Fold change	Gene name	Fold change	Gene name	Fold change
NR2F2	-7.3	LOC100132593	-15.7	ASB9	-46.2		
FAM5C	-7.4	SFRP1	-15.8	DMRT3	-50.7		
CR936711	-7.6	EFNB2	-15.9	BEX2	-53.8		
ME1	-7.6	LMO4	-16.0	STXBP5L	-54.2		
RERG	-7.6	SYNE1	-16.1	LRP1B	-59.5		
THC2512148	-7.8	KRT80	-16.4	DCN	-61.9		
SC5DL	-7.8	THC2646628	-17.3	MGAT4C	-65.8		
STAMBPL1	-7.8	GSTO2	-17.8	VGLL3	-72.9		
HAND2	-7.9	ATRNL1	-19.4	RASSF9	-73.3		
CITED2	-8.0	HYLS1	-19.4	CHRNA9	-77.0		
CTSF	-8.1	EPHX2	-19.8	BEX1	-138		
RGS20	-8.3	DNAJC12	-20.1	PCDH20	-252		
P2RX5	-8.4	PPP4R4	-21.0				
ZDBF2	-8.6	CDCA7L	-21.5				
TMCO4	-8.6	PTPRK	-21.7				
IDO1	-8.7	CDH2	-22.0				
RBM47	-8.7	ARHGDIB	-22.2				
SLC38A5	-8.8	HAPLN1	-22.4				
CEP44	-8.8	GAD1	-22.5				
GPC4	-8.9	CELF2	-22.5				
TP53TG1	-9.0	C8orf4	-22.7				
IFI27L2	-9.2	MDK	-22.9				
METTL7A	-9.3	IGF1R	-23.1				
CHRNA3	-9.5	CGREF1	-23.8				
GLIS1	-9.5	SGCE	-23.8				
AB014766	-9.7	PDZRN4	-24.2				
GCH1	-9.7	BF217859	-24.6				
RIN2	-10.1	PAX6	-24.9				
CYB5R2	-10.1	RARB	-25.3				
ENST00000462693	-10.6	CYB5A	-25.5				
FAS	-10.9	GLCCI1	-25.6				
SESN3	-10.9	HTATIP2	-25.7				
ICA1	-10.9	THC2535223	-25.8				
MMRN1	-11.0	TMPRSS15	-25.9				
SP5	-11.0	TOX	-26.6				
FERMT1	-11.3	RERGL	-27.3				
NFIA	-11.6	KANK1	-27.8				
FUT4	-11.8	PLAC8	-28.5				
MCF2	-12.4	DOK6	-28.5				
AF100640	-12.4	EDIL3	-28.6				
PDE6H	-12.5	MLH1	-30.1				
EPCAM	-12.6	PEG10	-30.4				
EFHC2	-13.0	ABCA5	-31.8				
L3MBTL3	-13.4	LUM	-34.1				
TLE1	-13.4	GPM6B	-39.8				
LOC100505806	-13.5	NTS	-40.2				
SCIN	-14.2	HECA	-42.2				
RBM20	-15.4	FAM198B	-43.5				